Bullous Diseases

essential

65

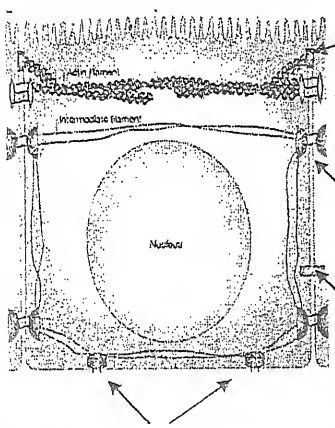
1. Basic: . Desmosome
   . Hemidesmosome & DEJ.
2. Autoimmune bullous diseases:
   . Intraepidermal blisters
   . Subepidermal blisters.
3. Non Autoimmune bullous diseases.

A. Basics

1. Structure of Desmosome:

. There are 5 Types of Cell (Keratinocyte) Junctions:

Five major categories of adhesion complexes are found in the epidermis.



Tight junctions – form at the apical end of lateral membranes forming extracellular diffusion barriers

Adherens Junctions – intercellular adhesion site linking actin cytoskeletal networks

Desmosomes – intercellular adhesion site linking keratin cytoskeletal networks

Gap Junctions – intercellular channels allowing diffusion of small molecules

Hemidesmosomes – adhesion site linking keratin cytoskeletal networks to extracellular matrix

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. the Most important are:

1. Desmosome : Join KCs & each other.
2. Hemidesmosomes : Join KCs & BMZ.

Structure of Desmosome

1. Inter Cellular Cement Substance (ICAM or Transmemb. proteins)
   - made up of Ca+ dependant Glycoproteins called "Cadherins"
2. Attatchement plaques (APs): (at inner side of cell memb.)
3. Cytoskeletal ptn. (inside the cell)
   - Keratins. (Keratin intermediate filament) (KIF)

هنا نتكلم عن تركيب جزء من أجزاء الـ Desmosome.

Adhesion complex	Transmembrane proteins (Cadherins)	Plaque proteins	Cytoskeletal proteins
Hemidesmosomes	integrin α6β4 BPAG2 (BP180)	BPAG1e (BP240) plectin	keratin
Desmonsomes (mediate slow)	desmoglein 1 desmoglein 3 desmocollin 1a, 1b desmocollin 2a, 2b desmocollin 3a, 3b	desmoplakin 1 & 2 Envoplakin, Periplakin plakoglobin plakophilin keratoclamin	keratin
Adherens Junction (mediate quick but weak adhesion)	① E-cadherin (P&E) ② Nectin	Catenins ← α, β, p120 Afadin vinculin VASP p120ctn	actin
Tight Junction	JAMS claudins occludins	zona occludins 1, 2, 3 MAGIs 1, 2, 3	actin
Gap Junctions	connexins 15 human genes GJα, GJβ, GJγ families	-	-

Cadherins: 2 Types (بولونك)

① Classical Cadherins: E, P, N Cadherins they are cadherins of Adherens J.

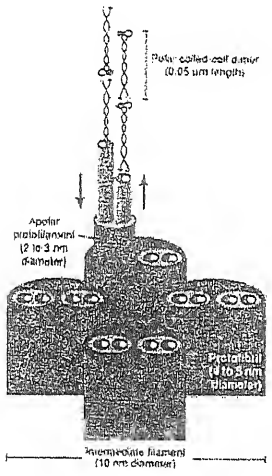
② Desmosomal Cadherins: DsG & DsC which are Cadh. of Desmosomal Junct.

Keratins (KIF)

- Keratins are the structural unit of KCs.
- Present in the form of filaments inside the cell & have 2 ends:
  1. outer end: → attached to ↓ APs.
  2. Inner end: → Lies freely in ↓ Cytoplasm towards the nucleus.

Keratins – gene family contains over 50 members

- mature keratin molecules have a diameter of 10-12 nm
- expressed in a tissue- and differentiation-specific manner
- keratins have conserved central rod domains and variable amino- and carboxy-terminal domains.
- Type I keratins are smaller and acidic; Type II keratins are larger, neutral/basic.
- keratin heterodimers further polymerize into larger filaments
- mutations that cause *major* defects in keratin molecular structure are non-viable
- mutations that cause *minor* defects in keratin molecular structure lead to major debilitating skin diseases.

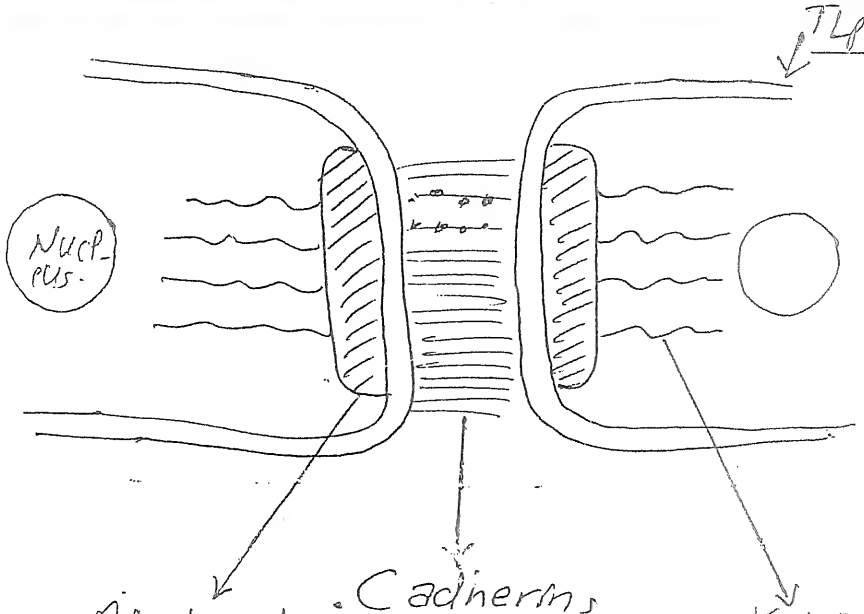


Tissue	Type I keratin expressed	Type II keratin expressed
✓ Basal cells	K14 (50 kD)	K5 (58 kD)
✓ Suprabasal cells	K10 (56.5 kD) K11 (56 kD)	K1 (67 kD) K2 (65 kD)
Hyperproliferative skin	K16 (48 kD)	K6 (56 kD)
Simple epithelia (also Merkel cells)	K18 (46 kD)	K8 (52 kD)

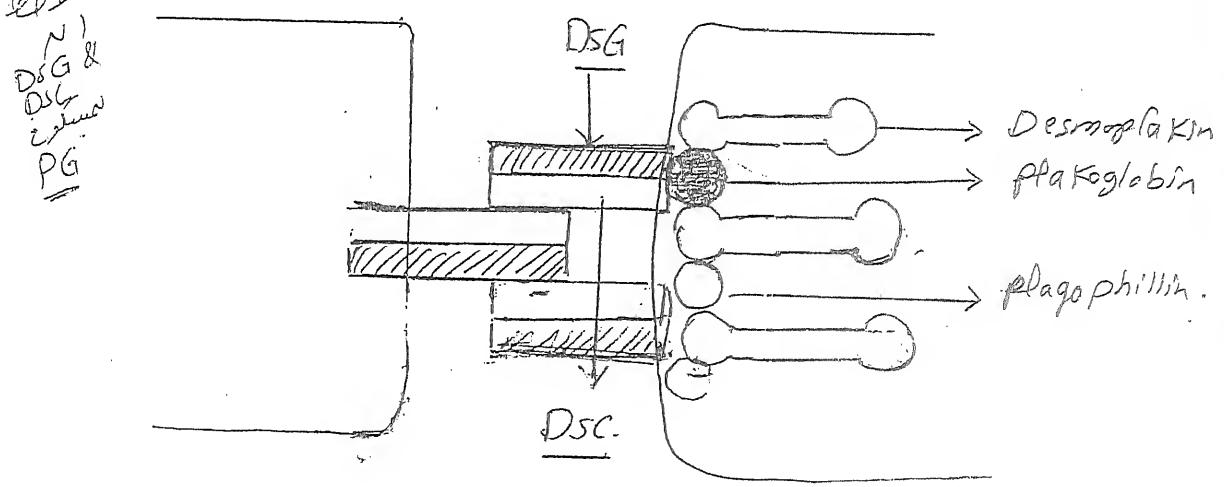
Genodermatoses Keratin mutation identified

Epidermolysis Bullosa Simplex K5, K14
Epidermolytic hyperkeratosis K1, K10
Palmoplantar keratoderma, epidermolytic K1, K9
Palmoplantar keratoderma, diffuse non-epidermolytic K1
Palmoplantar keratoderma, focal non-epidermolytic K16
Ichthyosis hystrix type Curth-Macklin K1

|| non epiderm. ↓ K16



- Attachment plaques (APs)
  - Desmoplakin (1,2)
  - plakoglobin
  - plakophillin I & II
  - Others: envoplakin & periplakin, Keratocalmin
- Cadherins
  - Desmoglein 1 2 3 4
  - Desmocollin:
    - 1 a&b
    - 2 a&b
    - 3 a&b
- KIF
  - Basal KC → K5 & K14
  - Horny → K1 & K10
  - prickle & granular: 2, 11
    - ٤ أنواع



- NB
  - DSG1 → is present in upper KC (More Superficial) So Autoantibodies against it → Superficial blisters [P.E, P.F]
  - DSG3 → in deeper KC (Suprabasal & Basal) Ab → More deeper blisters (PV, P. Vegetans)

- Skin Contains DSG I & III
- Neonatal skin & MM Contains DSG III only

- Function of Desmosome:

1. Cellular stabilizat⊃ (adhesion)
2. Signaling centers: by controlling cytoplasmic pool of signaling molecules (recently considered the mechanism of PV).
3. Plakoglobin: Has role in cellular prolif⊃ migrat⊃ & apoptosis.
4. Plakophillin: affect cytoplasm signaling pathways.

Bullous diseases

- Classification may be acc. to:

(1) Blister:
- Level
- Mechanism
- Infilterate

(2) disease Mechanism
- Immunological (Autoimmune)
- Non-Immunological (Non Autoimmune bullous)

- 1st Classification (dis. Mechanism or AEt.)

Immunobullous
- Epidermal Blistering diseases
  - Pemphigus family
- Subepid. Blistering diseases
  - Pemphigoid Family

non Immunobullous (4)
- EB
- SCPD
- H.H
- TAD (Graves)
- + (-ve DIF. & IIF)

Skin & Mucosal Biopsy in Bullous diseases..??

HP
- Vesicle: Early (To * bact. inf.), Small, whole, * area of intact skin
- Mucosal lesion → Edge of Erosion. (Intact vesicle)

DIF
- Perilesional Biopsy (Skin & MM)??
- Immune deposits are degraded in Blistered skin → false -ve DIF

(3) Classification According to level of Mechanism & Site of Blister formation.

Epid. → 3 Levels

Subepid. (See below)

① Subcorneal = Very flaccid Blisters (3 levels) + Crust

Acantholysis. | Cytolysis ✓ | Spongiosis

Cytolysis:
- SCPD (Net.)
- 2 Pemphigus (Neut.)
  - Foliaceus (IgG)
  - IgA (Neut) (SCPD Type)
- Others:
  - Bullous impetigo (Ne)
  - SSSS (-Ve)
  - Pust. Ps (N), ETN (E), Candida (N), Impetigo Non-Bullous (N)

Spongiosis:
- miliaria Crystallina (-ve)

② Str. Spinosum = Intraepid. = Flaccid Blisters

- Acantholysis → IgA pemph. (IEN type) (Neut)
- Cytolysis → Epidermolytic Hyperkeratosis (EHK); EBS / Viral
- Spongiosis (Intercell. Edema)
  - Fungal inf.
  - Eczema
  - TAD
  - Miliori Rubra
  - Incontinentia Pigmenti
- Intracellular oedema → Ballooning = Retic. degen. → Viral ✓ Blisters (HSV & VZV)

③ Supra basal (6) — "less Flaccid Blisters" (All ē Acantholysis)

3 Pemphigus:
- Vulgaris
- Vegetans
- PNP

Eosinophilic Infilt.

3 SLE:
- Dawser
- Hailey-Hailey (BFP)
- Grover (TAD)

(Scanty infiltrate) or (-Ve)

Pemphigus (Greek pemphix = Blister or Bubbles)

- Def → • Severe .. Even life threatening
  • Auto Immune
  • Intra epid. blistering dis
  • Ch. By < Acantholysis.
  Auto anti bodies.
  against Epid. cadherins (family of Ca-dependant Cell-Cell adhesion molecules)

- classifications (أنواع)

(A) Classical pemphigus

1. P. vulgaris → Subtype P. Vegetans.
2. PNP
3. P. Foliaceus → Subtype < P. Erythematosus. / P. Herpetiformis. / Endemic foliaceus.
4. IgA pemphigus.

(B) Other Variants:

1. Drug induced (P.)

2. Neonatal pemphigus

DIF: IgG (100% IC ± C3)

(Pemphigus Vulgaris)

- Age: Middle age (< 50 ys)
- Sex: M = F
- Race: More common among (Jewish.)
- Ass. HLA (A10, A26, BW38 & DR4)
- Clinically: △ Generalized flaccid blisters.
  - .. usually = Asympt or Tender > pruritic.
  - .. occur in NL skin → breaks easily → (denuded) areas that tend to ↑ in size & often become crusted
  - Post [.. Post. inflamm. Hyperpigm. usually present at site of Healed lesion ∴ usually (↓↓ BY Time)
  - .. No scarring Except if 2ry bact. inf.

Middle Age
Life long
H Threat.
Flaccid
Tender
NL Skin
No Scarring

△ Sites <

.. Skin: (Scalp) face, Trunk, axillae (*)
(Large amount of Pemph. Ag)

M.M: .. affected in > 90% of Cases.
- In 50-70%; The dis. start with mm affection before the skin. (Prodromal)
- usually presented ē: oral, pharyngeal, Nasal, Conj. Erosions (Not blisters)
  - (Bad general condit.)

△ +Ve Both Nikol. & Asboe Hansen Signs But (not) diagnostic.

.. Nikolsky's sign: firm / "sliding" press. on unaffected skin → Avulsion of l. outermost epid. Layers from l basal Layer .. & (±) blister formation.

- +Ve in: SJS/TEN & SSSS
- Indicates: Active dis.

Sheet
- Skin
- MM
- Histopath. (level & infilt.)
- Immunopath. DIF - IIF (antigen)

HEMORRHAGIC CRUSTS OF THE VERMILION LIPS
- Herpes simplex
- Herpes zoster
- Pemphigus vulgaris
- Paraneoplastic pemphigus (see ...)
- Stevens–Johnson syndrome/TEN spectrum
- Erythema multiforme major (see Fig. 3.11)

L.P. CP
FDE

Asboe Hansen Sign: Linear (Lat.) pressure over the surface of (a recently) developed blister → Peripheral blister spreading.

(Bullae Spreading Phenomenon)

Histopathology (Types)

- suprabasal Acantholysis (with) Eosinophilic infiltration & +ve Tzanck smear (Acantholytic "Rounded up" → Pemphigus cells in blister cavity)
- The basal cell Layer forms a row of "Tombstone" that form the base of blister.

Immunopathology: (DIF مناعي نسيجي مباشر)

(IgG4 doesn't fix Complement)

- **DIF** → 100% I.e. IgG + 50% C3, IgM (rare), IgA (±)
  (Perilesional Skin) (intercellular) (chicken wire at lower epid)
- **IIF** → 90% circulating IgG < 1/4 (more pathognomonic)

Pathogenesis

Target Antigens

Desmosomal Ags	Non Desmosomal Ags
• DsG III: • (100%) of PV cases • present in lower Epid. & MM (the Main DsG responsible for MM integrity) • Antibodies against it → Mucosal blisters & never limited skin lesions (DsG I in skin Compensate).	• ACetyl Choline Receptors Pemphegan • Annexin like (unknown pathogenic role).
• DsG I: • Attacked in 75% of PV cases. • present in all epidermis (sp.) & upper • Very little amount in MM (DsG III is the Main). ??	

(HL)

- Anti DSG-I Antibodies → No oral lesion but sub corneal blisters (DSG3 Compensate in MM)

  [This is called Compensation theory...]

<u>In PV</u> : <u>2 Immunoresponses:</u>

- (1ry response): Anti DSG III antibodies occurs first → Mucosal lesion at first
- (2ry response): Anti DSG III abs → exposure of previously sequestered epitopes → ++ Abs. production against DSG I → [2ry Immuno response] → so both Anti DSG I & III are present → Skin lesion.

(ده بيفسر حدوث الـ oral lesion قبل الـ Skin lesion)

- <u>this called</u>: [Epitope Spreading theory"]

- <u>NB</u> : (1) Inactivation of DSG1 by staph. toxins (Exfoliative Toxins Can → bullous impetigo & SSSS simulating PF).

  (2) Autoreactive T-cells may contribute to DSG3 attack by liberation of IL1 & TNF-α.

- <u>Causes of death</u>
  - <u>Erosion</u> → disturbed Epid. barrier → (Electrolyte Imbalance.
  - <u>2ry bact. inf.</u>
  - <u>Complications of H (e.g Cs).</u>

NB. <u>There are 2 Types of PV:</u>

① <u>Mucosal dominant</u>: only Mucosal affection

② <u>MucoCut.</u> Cut. & Mucosal affection

P. Vegetans

(Variant)

- **P. Vegetans:** Like P. Vulagaris in all things but differs in:

- Clinically, 2 Varieties:
  1. (Mild) = Pustular = Hallopeau type: "Pustular Eruption" (Pyoderma Vegetans دايبوى)
  2. Severe = Blistering = Neumann type: P. Vulgaris like.

"تكلم بس أصم الدي P. Vegetans أو بيدك P. Vulgaris وبعدين يبقى بعض vegetans → P. veget.

- the 2 types: → Crusted, Vegetating, Papillomatous proliferation (specially) on intertrigenous areas (also the scalp & Face).

DD
عرف الأمراض المتشابهة
- H. Hailey
- Pemphigoid Vegetans
- Pyoderma Vegetans

(NB) . usually start as PV →(on healing) Verrucous changes & Hyperk. with Pustules at the edge.

دارك . **Pathologically:**

- **Early:** as (PV)
  - Suprabasal Acantholysis
  - "Intraepid" Eosinophilic Microabscesses (hallmark).
- **Late:**
  - Hyperkeratosis.
  - Acanthosis
  - Papillomatosis
  - Pseudoepitheliomatous Hyperplasia (PEH)

. DIF, IIF, Targeted Ag & Tx as → PV.

(للعلم) NB
1. P. Vegetans: may represent reactive pattern of skin to the autoimmune insult of P. Vulgaris.
2. vegetating lesions may develops on top of P. vulgaris lesions (which are long standing & Resistant to Tx.) or develops de-novo.
3. (MM) may show "Cerebriform like lesions" (Invariable Involvement)

(DIF, IIF, Targeted Antigen & Tx → as P. Vulgaris)

Paraneoplastic pemphigus

" طلة بائسة "

(I.J)

onset of Tm:
- 70% at Diag. of PNP
- 30% after PNP

- Ass. with Bg or Mg Tms: Commonest:
  - Non-Hodgkins (40%)
  - Leukemia (Chr. lymphocytic) (30%)
  - Castleman's Tm (10%)
  - Thymoma (6%)
  - Sarcoma (6%)
  - Waldenstrom's Macroglob. (6%)

" Drugs: Fludarabine

- affect Elderly
- Skin: 5 varieties
  - P. vulgaris like: Flaccid bullae
  - B.p like: Tense bullae.
  - Targetoid lesions: EM like or TEN like (at PP)
  - Lichenoid lesions: Commonest in chronic course > blistering.
  - GVHD: like.

- MM (ulcer) 3 Ch: in all cases (100%), very Severe, persistent (> PV)
  - ulcerat. of:
    - Oropharynx → extend to Vermilion Border of lip (مميز عن PV)
    - Esophagus.
    - Conjunctiva → scarring.
    - Bronchioles → RD.

NB
Blisters & EM like lesions on Palm & Soles → differentiate bet PNP & P.V

- Histopath: mixture of:
  - suprabasal Acantholysis ē Eosinoph. Infilt. (PV like)
  - EM like (KC- Necrosis)
  - L.p like (lichenoid infilt.)
  - Interface Dermatitis (↓ + vacuolar deg.)

- DIF: as PV +
- IDIF: Intracellular (AP) (↑ Desmopl. Plako.), Inter Cellular (↓ DSG, DSC) & DEJ (BPAg 1,2 / plectin) deposit of IgG, C3, IgM, IgA.
  (Desmosome + DEJ)

Rat Bladder Sub. +ve

. **Targeted Antigen:** كثيرة

. DsGs (1&3) & Ds. Collins
. Desmoplakin, Plakoglobin, Plakophillin, envoplakin
. BPAg1 & BPAg2, Plectin.

. **Treatment:**
- if Bg Tm → disease Resolve if the Tm removed surgically
- if Mg Tm: → the dis. usually Fetal ē in 2 Ys Even after ttt of underlying Mg. (d.t Sepsis, MOF, Resp. Failure) +

. MM less responsive to ttt < skin.

(drug of choice) → Prednisone with or without:
- Cyclophosphamide (Cytoxan)
- Cyclosporine.

(٤ انواع)
. Classical
. Localized.
. Endemic
. Herpetiform

رقيقة

P. Foliaceus

Course
. chronic
. Better prognosis.

. **Skin:** . Very superficial blisters → Easily Eroded & Crusted (So: only Crust & Scales are seen) at (Face, Scalp, upper Trunk)

Intact bullae مش بتشوفيه
Crusts & Erosion لكن بتشوف

. No st. Corneum or granulosum in MM so "No DsG1"

. **MM:** rarely affected (Very little DSG1).

. **Path:** . Sub corneal blistering ē inflammatory Cells in the Cavity specially Neutrophils
. upper dermal Eosinophilic infilt.

(SubCorneal, Neut., Eos.)

خلي

* Crusts & Scales عاشان كدا بيقولوا عليه
The Commonest bullous dis that May → Erythroderma.

* DIF & IIF → as P. vulgaris (but subcorneal deposits). → (upper epid.) (16)

. Targeted Ag: (DsG1)

P. foliaceous Varieties → P. Herpetiformis

• localized → P. Erythematosus [Senear-Usher Syndrome]

. crusted, scaly lesions on Seborrheic sites (Lupus like rash) — malar area, Face, interscapular & presternal

. DIF: as P. vulgaris ± Deposits at DEJ (+ve LBT of un involved skin)

. IIF: as p. vulgaris + ANA. (but -ve Antids)

• Endemic (Fogo Selvagem) — Generalized

. CIP: ① young children & adults (<20)

② d.t infectious agent Transmitted by Mosquito (Simulium sp.)

③ CIP: . Erythroderma . Bullous . prurigo like.

④ IH → moving to urban area (away from river)

. NB: the Term P. Erythematosus: was originally applied to patients having Immunologic features of Both diseases or patients have been reported to have the both. (+ANA; DEJ dep.; Cell. dep.)

• Pemphigus Herpetiformis:

. Clinically: Resemble (DH); pathologically: it is a Pemphigus (F. or V.)

DIF & IIF

. Considered as: P.F variant (+++) / P.V variant (+)

• skin: Grouped, Severely pruritic, Erythematous (vesicular, Bullous, Papular) Eruptions & Herpetiform Pattern

DH → Dapsone

. Mm: (±) [± DsG3]

- DIF: PV or PF
- IIF: " "
- Ag: DsG1 > DsG3

(Intercellular IgA dermatosis) **IgA Pemphigus**

- Skin: 2 Types < SCPD Type / IEN Type (Intra Epidermal Neutrophilic)

Vesicles

IgA bullous diseases: 1. IgA pemphig 2. L ABD 3 DH

- Both types ch by: Flaccid vesicles or Pustules that tend to coalesce → annular or circinate pattern with crust in the center of lesion that has: **Sunflower like Pattern** → شكل زهرة

at

Axillae & groin (bl trunk & proximal Extrem. ± affected).

Pustules: IgA → ++ Neut.

- M.M: → (rare)
- Path: → SCPD type: Subcorneal Blisters. / IEN ": Sf. Spinosum Blistering
  - Neutrophilic infiltrate.
- DIF: IEN type: IgA_1 deposition in < lower / entire Epid.
  - SCPD ": " " " upper epid.
- IIF: Circulating IgA auto antibs (to) Epith. Cell Surface

Diff at from SCPD

- Targeted Ag (Heterogenous): IEN → unknown ± → Other Ags: - DsG1, - DsG3
  - SCPD → desmocollin (1)

- Neonatal Pemphigus:
  - occurs as a complication of maternal Pemphigus vulgaris (d.t passage of IgG)
  - Clp: → P. vulgaris
  - Resolve ē Catabolism of maternal Igs.
  - Neonate/skin Contain only DsG III (so neither ē PV is more dangerous in here term that PF).

Drug Related Pemphigus. (أدوية ضغط)

(A) Drug induced (Non Antigenic / thiol drugs)

(B) Drug Triggered (Antigenic / Non thiol / Amide Drugs)

Induced Pemphigus (-SH)

(Non Antigenic) [thiol drugs]

- Drug play the 1ry role.
- these drugs are:
  - Thiol drugs (sulfhydryl group) — Furosemide (Lasix) "لازكس", D. penicillamine, Captopril
  - Masked Thiols (Metabolized to thiol) — piroxicam, Penicillin, Rifampicine.
- (بحاوبه) Mech. penicillamine & Captopril contain sulfahydryl group (SH) (thiol) that interact ē (sulfhyd.) group of DSG1 & 3 → ?? direct interfer ē its adhesive functⁿ → Acantholysis (ēnt ++ Ab. productⁿ)

Triggered Pemph

(Antigenic) [Non thiol]

- ! Drug play a (2ry) role.. it induces P. in Presence of ! Major predisposing factors: — Endogenous, Genetic, Hereditary, Immunological.
- These drugs as: "Non Thiol or Amide" group
  ↳ Enal- & Eza pril
  - CCB
- Mech: the Drug acts as (hapten) + viral or bact. (or) endog. peptide → Form Ag → Autoabs → (attack DSGs)

	Induced	Triggered
IP	11 ms	4 ms
CIP	40% → P. F. 30% → P. Vulg.	P. Vulgaris or PE
M.M	18%	55%
	Spontaneous resolutⁿ ē in ≃ 6 ms. after Stop of Drugs.	persist even after drug discontinuatⁿ.

Captopril & D. penicillamin → Commonest thiols

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  - Masked Thiols (Metabolized to thiol).
    - Furosemide (Lasix)
    - D. penicillamine
    - Captopril
    - piroxicam
    - Penicillin
    - Rifampicine

Mech. penicillamine & Captopril contain sulfahydryl group (SH) (thiol) that interact è Sulfhyl. group of DSG1 & 3 → ?? direct interfer è ↓ adhesive Funct → Acantholysis (cell++ Ab. product)

Triggered Pemph

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  - Genetic / Hereditary
  - Immunological

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Captopril & D-penicillamin → Commonest thiols

Treatment of Pemphigus

- **Basic rule:** • PV is a chronic, life long dis. with Exacerbat° & remission → so ## (IS) For Control Not For Cure (No Cure)

- **Aim of ##:** (1) ↓ Antibody synthesis:
  - Cyclophosphamide → the most potent but has serious Toxicity
  - Cs → relatively potent & rapid (≃ 2ms)
  - other Immunosuppressives: less potent & less rapid (4-5ms)

(2) physical removal of antibs: by plasma-pharesis.

(3) Induct° of Catabolism of antibs: IVIG.

(4) ↓↓ inflamm. e.g. Cs.

NB: • the antibs. once formed & reaches the SK in the development of dis. become inevitable. Their degradative halflife is ≃ 3ws

↓↓ Igs → Existing (by degradat°) / Newly Formed (Immuno-Supp.)

• improvement occurs only ē reduct° of both existing & newly formed antibodies → so improvement occurs very slowly unless Antbs. are physically removed (by pharesis) or by inducing their Catabolism (by IVIG).

• Cs: the Major Cause for morbidity & Mortality in PV if used in large doses.

1) life long ## (For control)
2) Combat Therapy (Cs + others)

• ولذا فإن القاعدة العلاجية هي:

Use of Combinat° therapy:

Cs (to give Quick act°)
+
other immunosuppressive (steriod sparing to avoid Cs. S.E)

lines of Rx

- **1s line therapy**
  - Systemic Cs
  - لازم نيجي معاها
  - "Steriod sparing" (2nd line)
- **2nd line**
  - Azath.
  - M M
  - MTX
  - Ciclosp.
  - Cyclo-phosph.
  - Chlor-ambucil
- **3rd line**
  - Nicotinamide
  - Tetracyclines
  - Trental
  - Dapsone
  - Salazopyrine
- (مهم) **Rx of resistant cases**
  - Pulse Cs
  - Cyclophosphamide
  - IVIG
  - plasmapharesis
  - ECP
  - Biologics ↓ (Rituximab)

Systemic Cs in PV.

- **Continous oral Cs** (1st line)
- (مهم) **Pulse steriod** (2nd line)
  - rapid control
  - no need for long term Rx
  - So ↓ S.E.
  - IV Methyl prednisolone pulse
    - 1gm IV drip over 2-3 hrs for 3-5 days
    - ± repeated every 2-3 ws if needed.
    - (Cover 3 hrs for 3ds / 3w)
    - [under cardiac monitoring].
  - (مهم) IV/IM Dexamethasone
    - 100 mg daily for 3 ds / month.

Pulse (CDP) — Cyclo, Dexa. pulse — 500 mg/month.

• Most Recent Regimen:

1-1.5 mg/kg/d prednisolone for: 2-3 ms (or 6-8 ws) — (100-120 mg/day) يحفظ جيدة

غالبا خلال هذه الفترة يحدث تحسن

خلال هذه الفترة هانضيف
- Azathioprine or
- MM

Improvement
(if clinical & Lab.)

↓

قد ايه ؟؟ وكل ايه ؟؟ — نسحب ال Cs

- withdrawal every 2-4 ws (in less serious dis (1-2 ws))
- 1. طريقة كبيرة
  - 100 - 60 mg —اسحب بـ→ 20 mg decrements
  - 60 - 20 mg → 10 mg " " "

↓

at 20 mg
There is 2 methods
For withdrawal

Classical Method (1/2-4 ws)
- 20 - 10 اسحب 5 mg (في الأمراض الخطيرة)
- < 10 mg اسحب By 2.5 mg (or better 1 mg)

till 5 mg → Then Measure serum Cortisol level; if > 10 µg/dl; so HPA is functioning → Stop Cs. or in serious life long diseases (PV) → كمل لآخره

تكملة Alternate day regimen.
- لما توصل ٢٠ - ٢٠ مجم
- ✓ لازم الجرعة تكون صباحا
- Cs مع NSAIDs علشان تخفيف اعراض withdrawal symptoms أثناء day off

• Better release of:
- HPA
- CMI
- WBCs
- K⁺ exc

No improvement
↓
Consider resistant case e.g.
- plasmapharesis
- IVIG
- Rituximab (375 mg/m² once weekly for 4 weeks)

Alternate day therapy
(• day on • day off)

لازم تكون جرعة (20-30)

(طريقة)
- [A] 20-20 then 40-0
  - ونقلل الجرعة من ال day on
  - بمقدار 5 مجم كل اسبوع
- أو
- [B] 20-20 ثم 25-15 then 30-10 then 35-5 → 40-0
  - → نقلل 5 مجم للدوز EOD (زي ما شرحنا قبل كده)

• Assement of response or improvement
1. Clinical (كل اسبوع) < Healing of old lesions / absence of new lesions.
2. lab: ↓↓ Ig titer. (IDIF)

• NB on Cs:

(A) Mechanism of Action:

1. Antiinflammatory
2. Ig (↓ synth. & ↑ Catabolism).
3. # Macrophage Function & Lymphocyte Migration.
4. Stabilizes the lysosomal memb.

(B) SE:

Oral Cs.

- Salt & Water retention & HTN.
- DM
- Disturbed Fat & protein Metabolism.
- GIT irritation & ulceration
- ! Activation of dormant inf. e.g TB, HCV, HBV.
- **Osteopenia & Osteoporosis**

• The S.E Can be ↓↓ by:

- Pulse Rx
- Combination Rx.

IV Pulsed MethylPrednisolone

(خطر كثير شوية ع د جرعة عالية)

- HTN
- MI.
- Seizures.
- Electrolyte Imbalance.
- Sudden death: ± d.t < arrythmia or Pancreatitis.
- W.t gain
- Moode change
- GIT irritation
- Facial flushing.

> **قاعدة مع Cs**
>
> لما نيجي ما نشيل عليها كلام:
>
> 1. Prevent Pneumocystis Carinii Pn. by:
>   - Dapsone or Septrin.
>   - vaccination (Pneumococcus)
> 2. Prevent Osteopenia & Osteoporosis:
> 3. H2 Blocker
> 4. حمية ملح

Steroid induced osteopenia

- Diagnosis: DEXA scan (Bone mineral density study). before Rx → then → Every / year.
- Rx <
  - Prophylactic (No renal stones بشرط): → Vit D (400–800 IU/d) + Ca+ (1500 mg/d)
  - Curative:
    - ♂: Testosterone (if level is ↓↓)
    - ♀: Est. & progest.
    - also:
      - Bisphosphonate [as Allendronate]
      - Intranasal Calcitonin.

Allopurinol

A Zath. → 3 Metabolite → Xanthine oxidase, TPMT, 6 Thioguanine. } inactive

6. Thioguanine

(1). Antimetabolite → DNA & RNA → T cell & B cells. → ↓ LCs

(2) Anth Cox → used in AD.

- Interact

(1) Allopurinol → -- Xanthine oxidase → ↑ 6-thioguanine (So ↓ AZath. level if ē Allopurinol)

(2) ↓ level → OCPs, warfarin.

- Pregnancy D.

2nd line therapy

(Immunosuppressives / Cytotoxic or Steroid sparing agents)

- **Include:**
  - [Azathioprine
  - Mycophenolate
  - " Mofetil (MM)] → (الاهم)
  - MTX
  - 3C:
    - Ciclosporin (Cyclosporine) الاسم الشائع
    - Cyclophosphamide.
    - Chlorambucil.

- **Mechanism:**
  - Antiinflamm.
  - Immunosuppressives.

- **Indications:**
  1. Failed improvement sufficient for tapering
  2. Flaring during Tapering (> 3 ms)
  3. development of Cs S.E
  4. routinely used with Cs in all pts. ē Mod-severe dis. (as a sparing Agent)

  "الكورتيزون بيظهر بعد ٤-٥ شهور او اكتر
  علشان كده مش بينفع بنديه".

المسؤول عن (Metabolism)

1. Azathioprine (Imuran®) (50mg)

Mechanism	Dose	SE.	Monitoring
1. Antimetabolite & Immunosupp. (↓ DNA synth) 2. Act on B Cells 3. ↓ Cyclooxygenase enz. (so used in AD). Anti [Metabolite, B, COX]	قبل ما تديهاله لازم تقيس انزيم: • thiopurine methyl Transferase level (TPMT): . NL absent in 11 % of people . high level: Aza. 2.5–5 mg/kg/d . low level enz.: Azath. 1–3 mg/kg/d	[BM toxicity (if ↓TMPT) . hepatotoxicity] [Severe Nusea. . Fever] . Mg. (Leuk. & Lymphoma).	1. thiopurine MT (كل ٤ اسابيع) 2. CBC: (platelet) كل اسبوعين 3. LFTs: أول شهرين . بعدها كل ٤ اسابيع . كل اسبوعين لمدة شهرين . كل شهر لمدة ٣ شهور . كل ٣ شهور

Pregnancy (D)

2. Mycophenolate Mofetil

(Cell cept ® 250 mg 500 mg

Mechanism	Dose	SE	Monitoring
• Antimetabolite & Immuno-suppressive	1-3 gm/d or 35-45 mg/Kg/d	• GIT: Nusea & Vomiting • Hepatotoxcity & BM. toxcity: (rare) • Lymphopenia "without" Neutropenia *** (good sign ē #). • Pregnancy (D)	• CBC • LFTs.

NB [• Very safe
[. very expensive
[• Efficacy (±)
[. Slow onset of ACT

---

3. MTX :→ • Not Commonly used (± aggravate oral lesions of PV).
• 7-20mg/w.

4. Ciclosporin A:
• Mech. ← -- calcineurin
-- Ig Product (through -- CD4)
↓ IL4 & IFN γ → ↓ Ig.

• Not Effective in PV or PF but effective in PNP specially those ass. with Lymphoma (or) cHL lichenoid Erupt.

5. Chlorambucil:
• rarely used.
• Considered a substitution of Endoxan (cyclophosph.) If Hgic cystitis occurs.
• S.E: Cytopenia (unpredictable that may take months to resolve).

(HL) 6. Cyclophosphamide (Endoxan)® Cytoxan

(Alkylating cytotoxic)

[Alkylating agent from Nitrogen Mustard family]

Can be used as

→ Immunosuppressive "B cell > CD8 > CD4" (Cell cycle Independent cytotoxic.)

↓

1. DNA cross-link
2. Depurinate
3. Cleaved Imidazole ring.

↓ Induces remission

- Daily oral 2.5 mg/kg/d

ويأخذ يا مريض الصبح وبعده كمية ماء كبيرة (٦ أكواب ماء)

to wash its Metabolite → & prevent H.gic Cystitis.

NB. durable remission in 18-24 ms

. the method ↑ risk (5-10 times NL population).

→ Immunoablative (remove & destruct the ↑ cell population)

↓ Induces "Cure"

(but this Cure remain only for 2 ys → limit its use as Immunoablative).

. Mech.: wipes all clones of cell producing antibodies.

. Indication:
- Severe resistant PV
- PNP
- SLE.

. Regimen: Single, Very high "ablative" dose:

. IV (200mg/kg) /day for 4 days → upon recovery from BM suppression → Cure (or prolonged remission).

الطريقة بالتفصيل:

١. يتم حجز المريض في وحدة زراعة النخاع

٢- يوضع قبل العملية بتغطية مضادات حيوية (Vancomycin & Ceftazidime)

٣- IV 200mg/kg/d x 4 days

٤- يعطى مجاناً

(i) MESNA : 3gm in ½ liter over 2hrs /6hrs. (organo-sulfur compound)

(ii) Very strong Antiemetic (Zofran).

(iii) G-M-CSF

(iv) Erythropoietin 4000 U SC

(v) Packed platelet (if ↓↓)

Cyclo
Cyclophosphamide
Cancer
Infect.

• S.E:

1. ↑ risk of Cancer < Leukemia / Lymphoma / Cancer Bladder
2. Hgic Cystitis ⟶ Cancer (if Hematuria → Stop) d/t Acrolein Metabolite.
3. Sterility (♂) & Amenorrhea (♀)
4. profound BM suppression.
5. pregnancy: (D)

. Monitoring: CBC & urine analysis / week.

. NB: Cyclophosphamide is preferred as ↓ Neutropenia ass. with its use is predictable in onset & withdrawal of the drug ⟶ rapid recovery (in 7-10 days).

• European Guidelines (2014)

P. Vulgaris

- Mild → Cs alone
- Severe → Cs + Immunosup. (Steroid Sparing)

• 1st line:

. Prednisone 0.5-1.5 mg/kg/d

. Taper by 25% of dose Biweekly & of < 20mg

Taper more slowly

- give — proton pump — H2 Blocker — Calcium.

• 2nd line: Azathioprine & MYCophenolate.

. 3rd lines: MTX, IVIG, Cycloph., Dapsone, ...

Other lines of ttt:

1. Nicotinamide.
2. Tetracyclines
3. Tretinoin
4. Dapsone
5. Salazopyrine

A. Nicotinamide (& Nicotine patch smoke):

* Mechanism:
  1. -- Neut. & Eos. chemotaxis.
  2. -- Histamine release.
  3. -- Lymphoblast formation & Activation
  4. ↑ Acetyl choline release & production by -- ACH esterase enz. (cholinomimetic).

5. Cholinomimetic

- Dose: 0.5gm 3 times / d.
- S.E:
  - Headache.
  - Flushing
  - Flue like symptoms
  - Vomiting.
  - Hepatotoxicity
  - AN, pruritus
  - Ichthyosiform changes.

- Uses in Dermatology:
  - Behcet
  - Aphthus ulcer
  - Acne V.
  - P.V
  - Chilblain.

Both Treat pellagra.

(1). Nicotinic acid = Niacin = Vit B3 = Nicotinyl Alcohol.

- Uses
- ↓ lipids & VD (Antihypercholesterol)
- S.E: flushing

(2) Niacinamide ⇒ Nicotinamide:

No flushing nor ↓ lipid. AV BP.
- Antiflamm.
- Topically → Bleaching

NB: Niacin $\xrightarrow{Vivo}$ Nicotinamide

2. Tetracyclines: (2gm/day)

- Mechanism:
  - Antinflammatory
  - -- Neut. chemotaxis.
  - -- phagocytosis
  - --- cytokine product
  - -- MMP. (بطء كل)

3. Mestinon:

- Mech. → -- Choline esterase → ↑ ACH.
- Dose: 60 mg 1d.

4. Dapsone:

- Antinflammatory.
- ✓ of Choice in IgA pemphigus & P. Herpetiformis

5. Gold therapy:

- Alternative for long term Cs & Immunosupp.
- Dose
  - Test: 10 mg IM.
  - 1w later: 25 mg IM
  - then: 50 mg 1W (till) ← improvement ↓ Ig level, Toxicity, total dose 1 gm is reached
  - Mantenance: 50 mg/ 2-4 ws.

- Oral Type called Auranofin
- IM:
  - Thiomalate
  - Aurothioglucose

- S.E:
  - BM --
  - GN (Immune Complex Mediated) (glomerulo neph.)
  - Lichenoid dermatitis.

6. Trental: Anti TNF / 400 mg X3/d.

7. Tranilast:

- Mech. . Anthranilic acid derivative
  - . ↓ Histamine release by mast cells.
- Uses: · AD · PV
  · ECZema · Sarcidosis.

Treatment of Severe / resistant PV:

أهمية
. IVIG
. plasmapheresis
ECphotopheresis
. Immuno-ablative
. Rituximab.
. pulse Cs

1. IVIG → see TEN
2. plasmapharesis
3. Extra corporeal photopheresis [ECP]
4. Immunoablative ttt
5. Adjuvant Immunomodulators:
   - Rituximab
   - Tacrolimus (prograf)
   - M. Mofetil
   - pulse steroid

---

① IVIG → see TEN

② plasmapheresis: تعريف

. def. the only method to wipe out all pemphigus antibodies from circ.

. Technique: the blood is removed out of body → plasma is removed (separated) → Treated → returned to / body.
(بحاز زي بتاع الكلى)
↓ antibody removed. (Immuno-adsorption).

NB, in plasma exchange: plasma is separated → discarded → replaced by donor plasma, Albumin or Albumin + saline.

Complication:

. Minor
- Fever.
- Chill.
- Allergic reaction.
- Transient Hypotension.

. Serious
- Fluid imbalance ē pulm. Edema.
- depletion of platelet or clotting factors → Bleeding & inf.

-. pulm. Ed.
. Coagulopathy

Disadv.

1. Immediate ↑ in anti pemphigus antibodies which are produced in extravascular compartment (false transient ↑↑ → frequent repetition of plasmapheresis EOD).

2. Depletion of antibodies from circ. → ++ more Igs production (-ve feed back) → exacerbation of ds. in the 1st (few ds — 2ws) after 1 session

↓ avoided BY

Combined Plasmapheresis

+

"Pulse Cs or Endoxan"

or Any other Immunosuppressives.

لازم نعطيهم ٢ خلال ٤٨ ساعة بعد الجلسة

(So) Combine pulse + plasmapheresis → the best way inducing remission.

عدد الجلسات
ليوم للبرتوم
لغة اوصات
وتاد.

. plasmapheresis can be used in:

- Behcet
- Wegners granulomatosis
- Cryoglobulinemia.
- Antiphospholipid synd. (APS)

3. Extra Corporeal photopheresis:

Def. photoinactivat⁻ of WBCs ē 8MOP & UV in ♀ UVA (PUVA) in an extra corporeal system then reintroduct⁻ of damaged WBCs → ++ clone specific immune response → down regulat⁻ of activity of pathogenic cells.

@ As in plasmapheresis: should be combined ē Immuno-suppressors.

Immunoablative ##

1. Old Method → BM rescue → Eliminat⁻ or destruct⁻ of RES cells by busulphan or irradiat⁻ → reinoculat⁻ of stored BM

2. Recent Method: large dose pulsed Endoxan.

P. Foliaceous:

- Localized → Super potent Cs ✓
- Generalized → ## as PV.

Paraneoplastic

- Bg Tm → .. ??
- My Tm → ... ??

IgA P. → Dapsone (others):

- Sulfapyridine
- Etretinate / Acitretin
- PUVA
- Colchicine.

P. Herpetiformis → Dapsone.

Hemidesmosome & DEJ

الجزء الثاني من الـ Bullous

① Maintain the dermoepidermal adhesion ⟵ NL Skin & Wound Healing.

② Mesenchymal-epidermal interaction.

③ Mechanical support.

④ Selective permeability & Physical barrier.

- Adhesion
- Interact°
- support

1. Structural Component

KIF = 5, 14

① HD = Hemidesmosome · Consists of:

- inner plaque → ! Most Cytoplasmic Parts that Ass. ē KIFs
- outer plaque → Ass. ē basal cell plasma memb.

Consists of

- Basal cell plasma memb. → جزء من الخلية
- Sub basal dense plate: it is an extracellular component that lies ⊥ to & Just beneath the outer plaque & Ass. ed basal plasma memb.

HD 3 domains:
1. Cytoplasmic IAP
2. Membranous: CM
3. Extracellular domain: sub basal d. plate.

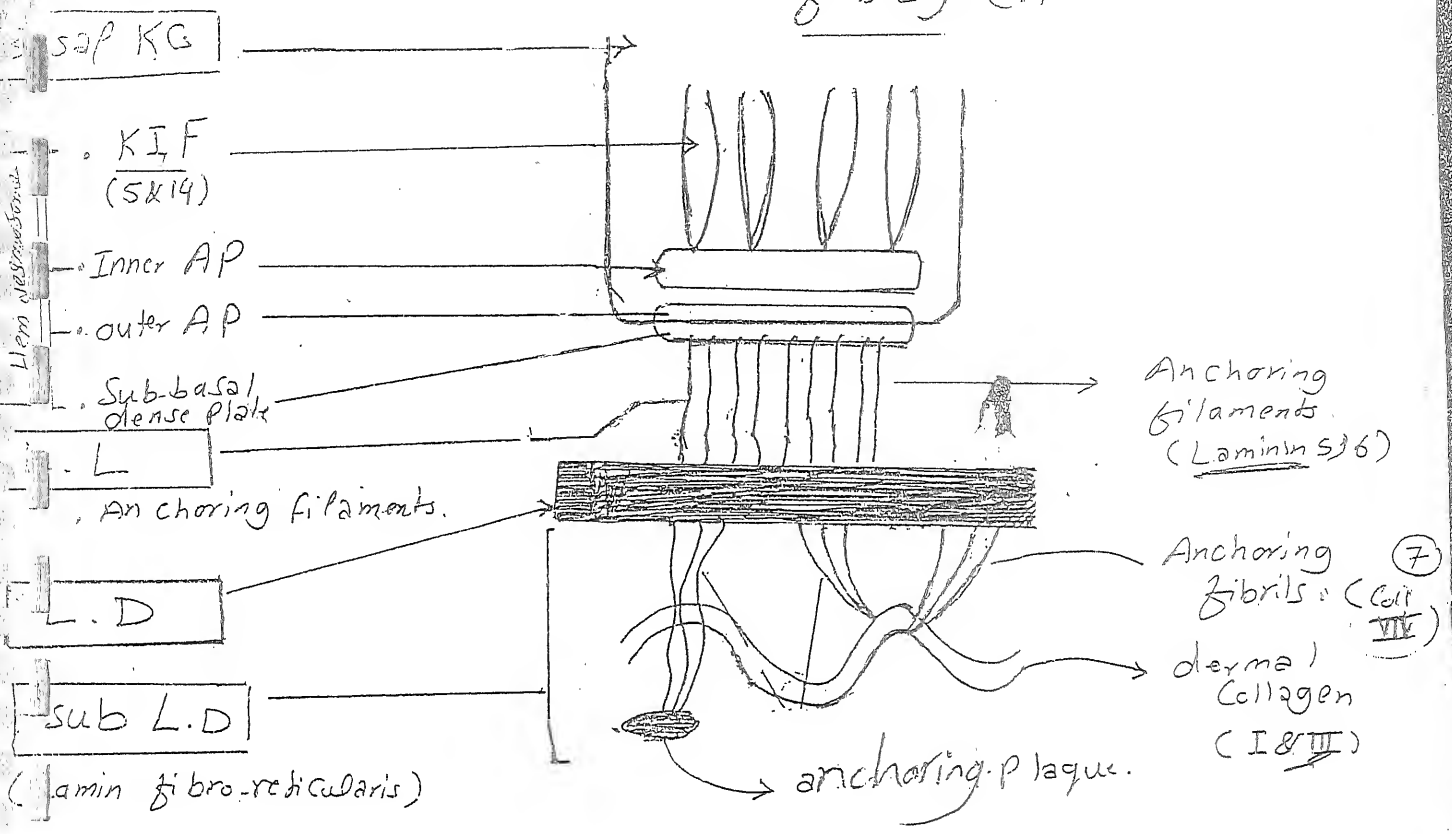
② L.L (Weakest Part of DEJ).

- Electron Lucent band (20–40 nm)
- Traversed by anchoring filaments ... (مرساة - ثبت)
- form areas underlying H.D (to) L.D.
- Anchoring Filaments extend from HD to LD.

③ L.D → · Electron dense band (30–60 nm in width)
· (E) barrier/filter that restrict passage of Molecules but can be Penetrated by MC & LCs.

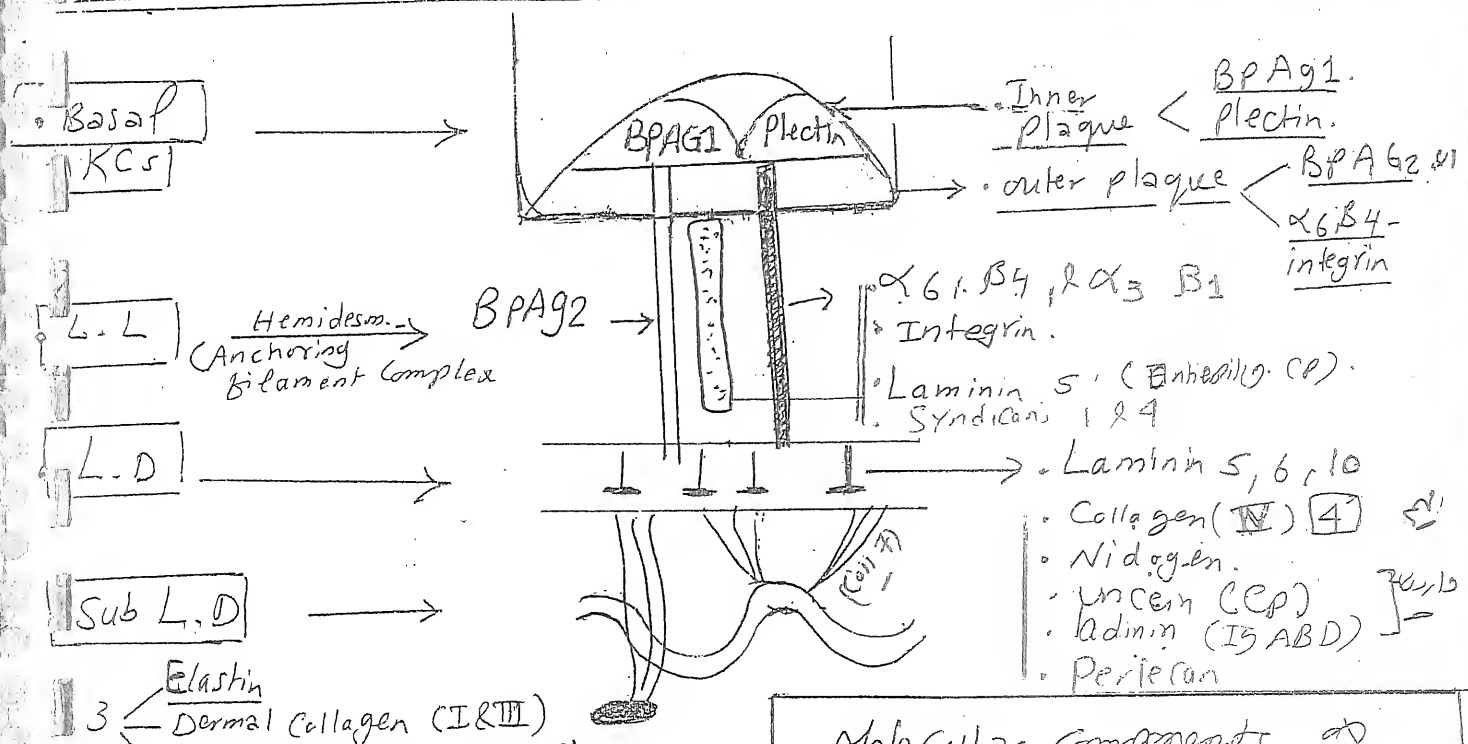
④ Lamina fibrorecticularis = Sub LD:
Traversed by « Anchoring fibrils » that extend.
↓
Formed of Type VII Coll.

• Structural Components of DEJ (Hemidesmosome)



Dep: (Hemidesmosome & Basal KCs → L-L → LD → Sublamina densa).

Hemidesmosome. Anch. Filament Complex.



from lower aspect of L.D &

Either ← Loop back into L.D or

insert into "Anchoring plaques" (Electron dense structures)

Note

Anchoring ← Filaments
Fibrils
plaques.

II Molecular Component

(1) HD: (3 parts as Desmosomes)

1. Cytoskeleton: KIF → K5 & 14
2. plaque proteins: (2) [IAP]
   - BPAg1 (230KDa): attached to KIF above & BPAg2 & integrins downward. / its deficiency ↓ not harmful
   - Plectin: present in KCs & ms. Type of desmoplakin (present in D. & HD).

OAP & L.L → 3. Transmembrane protein: (2)
   - BPAg2 (180KDa)
   - Integrins (α6, β4) (its intracell. domain)

(2) L.L (Anchoring Filaments).

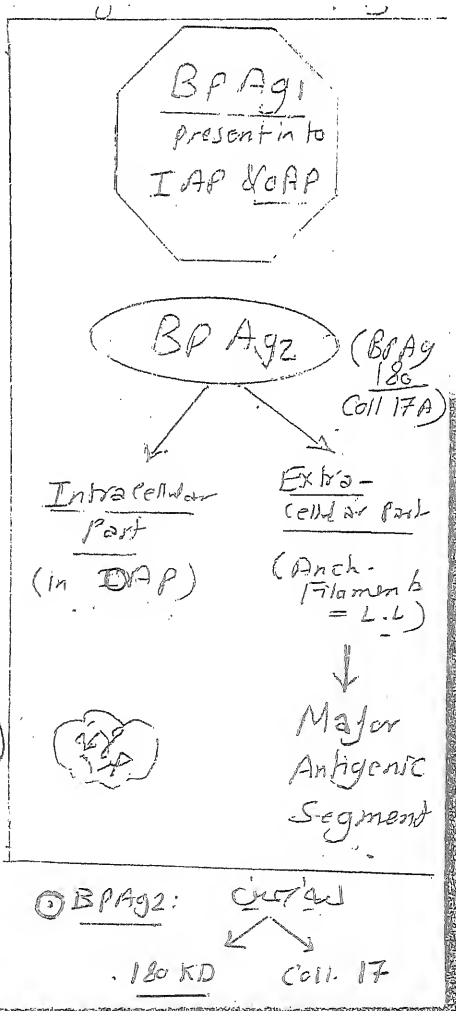
- BPAg2 (Extracellular domain)
- Integrins (α6, β4 domain).
- Laminin 5. (Epiligrin).

(3) L.D

- Collagen IV (↓ ← hematuria, RF, Eye manifs)
- Laminin 5, 6, 10
- Nidogen. (Ent)

(4) Lamina fibroreticularis (SLD).

- Dermal Collagen I & III
- Anchoring Fibrils → Collagen VII
  - Binds lamina & LD to AP.
  - ↓ exp
- Elastin.



① BPAg2: Cut'ed
- 180 KD
- Coll. 17

Subepidermal Blisters (level & Infilt.)

Basalar (Separation bet L.L & cell membrane of basal KCs or bet. L.L & Sub-basal dense plate)

1. d.t Basal cell degeneration diseases (Lichenoid dermato.)
2. others: EBS & HG.

Intra L.L

٥ أمراض

- (E) [. B.P. / . HG]
- . CP (-ve)
- . DH
- . LAD (+++)

→ (N)

٣ أمراض

- . JEB
- . EBA (±)
- . PCT

Sub L.D

٢ أمراض

- . EBA (++)
- . BsLE

→ (N)

٤ أمراض

- . DEB
- . LAD (±)
- . CP (Anti-laminin)
- (M) . Bullous mastocytosis.

(N) Neutrophilic Infilt.
(E) Eosinophilic "
(M) Mast Cells.

هام (Some important infiltrations)

① . **Neutrophilic**

- . IgA Pemphigus
- . EBA
- . BsLE
- . CP
- . DH
- . SCPD
- . impetigo contagiosa
- . Candida
- . Pustular ps.

② . **Eosinophilic:**

- . HG
- . BP
- . 3 Pemphigus ← Vulgaris / vegetans / PNP.

③ . **Lymphocytic** → Viral blisters.

④ . **Scanty or Absent**

- . ٣ أمراض ← Darier / Grover / H-H
- EB
- . PCT
- . Bullous impetigo
- . SSSS
- . Miliaria.

⑤ **Mast Cells** → Bullous mastocytosis.

الأهم: ① ②

خلاصي
(Emed 2011)
Belgnih

Sub Epidermal Blistering diseases

(See 1 Classificati)

"Bullous pemphigoid" (B.P)

- Def → chr., Bg, self limiting, auto immune Blistering dis. ch BY formation of Subepid blisters.

- Age > 60 ys.
- Sex: equally affected.
- Ass: (مسبب الرفا)
  1. Autoimmune dis. e.g SLE
  2. UVB & PUVA (photo therapy)
  3. Frusemide, ACEI. (Drugs)
  4. Mg (Para neoplastic). شفوي
  5. Neurological disorders.

لو بيوصف BP في سكن For Mg. ??

- Bg
- Self limiting (5-6 ys)
- > 60 ys.
- ± ass

- C/p: Tense Blisters:-

Skin

- usually localized to flexures. (but ± generalized)
- on NL or Erythematous skin. (Erythem. > NL)
- first → Empty; then filled c Cloudy fluid & ± Hgic.
- ± Rupture → Erosions & Hyper pigm. (No) scarring or milia.

- -ve 2 Signs: < Nikolsky's, Asboe Hansen.

شفوي
Prodroma of B.P → ± Preceded by: (Early or prodromal BP):

- Erythematous patches
- urticarial plaques
- Targetoid lesions

→ later Bullae

"شفوي" lasting > 24 hrs →

- Itching, moderate - Severe.

MM → Involved in about 20% (mixed & Transient) (rare). (3e)

Clinical Variches (13)

- Localized type:
  - Oral & Acral (Infants).
  - Vulvar (sp. girls)
  - Pretibial (Commonest site of Localized BP is Shin)
  - at sites of: irradiation, PS. or "Burns".
- Generalized: affect flexural areas or whole body.

- Bullous: (classical).
- Non B: No Bullae but: Erythematous Patches, urticarial plaques, Targetoid lesions → "prodroma"

Urticarial Stage of B.P: enter in DD of persistant urticarial lesions > 24 hrs. → as urticarial Vasculitis

- Vesicular

- P. Nodularis: (Prurigo Nodularis like but ē Blisters).
- Pemphigoid Vegetans: (Similar to Pemphigus Veget but Immunopath of B.P).

- dyshydrosiform: (dyshidrotic Ecz. like at palm & soles = pomphylex).
- Erythrodermic (similar to Eryth. Ps.)

- L.P pemphigoides: (See L.P)
- Anti P 105 pemphigoid: (Severe)
  - Ag: 105 KD (Protein: in L.L)
  - CIP → acute onset. P.V(or)TEN like severe oral
  - DIF: Linear Ig G & C3.

Anti P 200 Pemphigoid.
200 KD Protein autab.
Recently Called: Anti-Laminin γ1 Pemphigoid

- Childhood B.P: ch BY
  - Associated ē Vaccinal ^
  - Acral (Face, Hands & Feet).
  - Course < 1 y.
  - Remabl: Acral or Generalized.

childhood ↑ < 1 y.

- Prognosis of B.P:
  - usually self limiting ē in (5-6 ys)
  - some pts may die ē in (6ms - 1y)
  - may be d.t ⁄ ass. diseases.
  - MR: statistically Higher in Anti BPAg2 Cases > BPAg 1.

- Pathology: (intra L.L ē Eos. infi. pt.)
  - Sub epid. Blisters (intra L.L) → By EM
  - No Acanthelysis (Intact Epid.)
  - Eosinophils in → Blister Cavity / upper dermis (infi. pt. is predominant ē Poly morphous Eos.).

- DIF: 100% → linear C3 (poly); 80% linear IgG1
  (Linear) at L.L.

- IIF: 80% → Ig G (mainly IgG1)

- Targeted Ag: BPAg2 (+++) (Collagen XVII 180kd) & BPAg1 (+) 230kd.

Can fix Complement (Not like IgG4 & P.V) → NCs ē similar C3 by DIF

* B.P may be ass. ē:
  1. Cancer (GIT, Bladder, Lung) so screening if the pt is → middle aged. / systemic manifs are +ve.
  2. autoimmune dis: SLE & IBD.
  3. ass. ē: PUVA, Lichen planus & Ps.
  4. Neurological disorders: MS.

Drug Induced B.P.

. PUVA

- Captoprip (ACEI)
- Enala prip
- Frusemide
- penicillamine ↓

Pemph. بيعمل
Pemphegoid

Tretment

↓

اعطي ع طول

Superpotent Topical Cs (Dermovate)

↓ Then if

Mild / localized dis: You Can Add

- Nothing: only Topical Cs
- Tetracyclines + Nicotinamide
- Dapsone
- Sulfonamides
- Erythromycin
- penicillin.

Severe / Generalized dis: Add

- Systemic Cs
  prednisolone 0.5-1 mg/kg
  1d → Controlled (usually in 2ws) → Taper over 6-9 m.
- Other Steriod sparing Drugs e.g. Azathioprine.

قاعدة

في كل الحالات لازم: Dermovate Cream.

← Control mild dis ↓ dose of Systemic Cs.

"Tarolimus" أو أخوه

. hard & Cranchy food: ممنوع الأكل

- Chips
- raw fruits
- Vegetables.

Herpes Gestationis (HG) / (Pemphigoid Gestationis; PG)

- Why So Called that:
  - Gestationis = Pregnancy Related
  - Pemphigoid: Has — Clinical, Histological, Immuno-Pathological "Similarity to B.P"

- Incid: rare ; 1:50.000 pregnancy. , 50% during 1st pregnancy
- onset: either during pregnancy: usually 2nd or 3rd (75%) Trimester.
  - or Postpartum:
    - (may occur or Exacerbate) (25%) = (75%)
    - i) early → after late preg. → Recur Postpart.
    - ii) 2nd or 3rd
    - iii) Postpartum
- Recurrence: 40%: with subsequent pregnancy
  - Cause: OCPs (25%)
    - menses
    - postpartum
    - VM or Choriocarcinoma.
- Course: resolut ± late pregnancy → Flare → Spont Resolut (Cons)
- Complication: (rare): (Fetal or Maternal)
  - Prematurity
  - HG ≥ fetus (3-10%; mild & self limiting).
  - ↑ MR.
  - BP
- Risk of relapse of Course:
  1. ↑ Age
  2. Susceptibility
  3. Multipl ++

- CIP: Severely Itchy Erythematous papules & plaques at abdomen (Specially periumbilical) → spread to involve Trunk back, buttocks & arms (2-4 w.) → Large, Tense bullae ± in annular config.
- NB:
  - Sparing: (Acne+MM) Face, scalp, palms & soles & MM (20%)
  - Some Cases: No Blisters, only Erythem. plaques

- Path. → as B.P
- DIF:
  - → 100% linear C3 (at L.L)
  - → 40% IgG
  - → Salt split skin: → Epid. side Fluorsc.
- IIF (25%): → "HG Factor" (Circulating IgG1 that binds To BPAg2 (+++) & BPAg1 (+))

- Pathogenesis: "مهم"

مش مهم دي

AbNL expression of MHC II at chorionic villi (of paternal haplotype origin) (HLA DR3,4, DP, DQ) → Imm R initiation against placental BMZ Ag (called HG Ag) [Immune Response (Anti HLA Abs)] → autoantibody production (IgG1) (Called HG Factor) That Cross React with skin BPAg2 → HG

- Treatment: ([illegible])
  - Bolognia → Cs (systemic) "أهم"
  - → others: (Emed 2010):
    - Other lines:
      - Emollients, Tepid baths & Compresses
      - Dapsone
      - Nicotinamide + Tetracycline
      - Plasma-pharesis
      - IVIG

Cs & pregnancy (C) — (Category C)
1st Trimester
Cleft Palate
others:
placental calcification
↓BW.

- mild dis: → Topical Dermovate + Antihistaminic
- Severe: → Cs.

(2011) Bologna

Cicatricial pemphigoid

(CP) (Mucous memb. Pemphigoid) خاص بمرض (39)

- Age: 62-66 Y.
- Sex: M > F = 1:2
- Remission: less incid < B.P

هو اصابة الـ MM وتعلقه في حالات نادرة جلد (%25)

chr. blistering dis. affects:

- Mainly **MM**
  - Mouth (local) — Gingiva > Palate > buccal (most common)
    - desquamative gingivitis & Erosions → Scarring (Reticulated L.P like)
    - (cotton tip & Blowing → peeling of Mucosa)
    - other MM: Nasopharynx, oesophagus, Genitalia. (LSA like of vulva)
    - Supraglottic → obst. → Tracheostomy.
    - Healing of oral: reticulate like L.P.
  - Eye (80%) [أهم ما يصيبه]
    1. Chr. conjunctivitis & vesiculation → corneal ulcer & scarring.
    2. Synechia
    3. Ankyloblepharon
    4. Entropion & Trichiasis.
- occasionally (25%) **Skin** — 3 Varieties
  - Localized (Commonest): Erythematous plaque(s) ē Tense Bullae & Vesicles (± Hgic): at Scalp / Face / Neck / Trunk ŵ are the sites of Recurrent Blistering → Severe atrophic scarring
  - Generalized (less common): Generalized disseminated lesions Resemble (B.P) → ± SLD
  - Brunsting-Perry pemphigoid: Elderly or affect the head & Neck without MM (Later → MM)

أوزي Mucosal oral Type ↑

- Pathology: Intra L.L Blistering ē mixed infilt or no infilt. (cell-poor) [oral → plasma cells]
- DIF: 80% Linear IgG & C3 (at) DEJ.
- IIF: 20-30% IgG1 (Low titer).
- Targeted antigen: Laminin 5, 6 — "anti-laminin CP" (Antiepiligrin) → SLD separation
  - BP Ag 1, 2 (+-+)
  - α6, β4 integrin → ocular CP

Commonest BP Ag2 & Laminin 5

(290)

- NB . BPAg2 : most Common Targeted Ag &
  → +ve salt split skin Technique at epid. side.

لكسى جزء تحته

عم الجزء

Salt split skin Tech. of CP
- Epid side: most cases → Anti BPAg2
- Dermal side: some cases → antilaminin CP

. Laminin 5/6 (Anti Laminin CP) (Laminin 332)

(٤ مرضى)

ch. By
- +ve Salt split skin Technique at the dermal side
- Mg associated. (Adenocarcinoma)

شغوى

Treatment

تدرس

1- Mild dis (localized) (oral/cut) → . as BP
- → (Cs < Topical / IL + Tetracycline oral wash)
- → Dapsone (1st line) or "Sulphapyridine"

2- Severe dis:
- ocular
- Laryngeal
- pharyngeal, Esophageal.
- resistant oral or skin to Topical IH

↓

Cs + Cyclophosphamide

NB: (1) CP sparser
- Infilt. by HP (cell poor)
- Immunoreactants
  - . DIF: 80%
  - . IIF: 30%

(2) Most Common Ags: . "BPAg2 & Laminin 5".
- α6, β4 → ocular CP.

(3) Cell-poor Bullous dis:
- . BP
- . EBA.
- . LAD.
- . PCT.

شفوى

(4) DD of Chr. Severe / Persistent oral erosion
- PV
- PNP
- CP
- LP

± SJS / TEN / EM.

تعريف

مع مقارنة

DH (Dermatitis Herpetiformis) (45)

(Duhring dis)

Def
- very chr (life long)
- Relapsing
- autoimm.
- Vesicular dis

⇒ "Considered as Cut. manif. of Gluten Sensitivity"

- **Age** → dis. of all ages (20–40 y)
- M > F (2:1)
- **HLA** < B8, A1 / DR3, DQ8
- **Ass.**
  - Common:
    1. GSE → 90% Asympt. ass. ē Mucosal atrophy & Intest. Lymphoma
    2. DM (Dermatoses)
    3. Hashimoto's Thyroiditis (25–50%)
  - Rare:
    4. Mg. (Lymphoma) (Enteropathy ass. T cell lymph).
    5. CAH.
    6. M.G.
    7. L.E.
    8. Diabetes.

× **Clinically** (No oral affect) — +ve oral but Asympt.

Adulthood DH

* **Eruption**
  - Polymorphic: < Papules / Vesicles < Bullae / urticarial or Targetoid lesions.
  - grouping
  - Bilat., Symm. on extensors:
    - limbs.
    - shoulders.
    - buttocks.
    - postaxillary folds.
  - Severely itchy (paroxysmal)
  - Healing: scarring & pigm.

Flaring: usually ē ingestion of Gluten or Iodide containing food.

Abdom. manifs: pain or diarrhoea, undernourishment.

Childhood DH

↓

as in adults + Palmar blisters or Brown macules.

> **NB**
>
> the clinic finding is Spont. Remission that lasting as long as 1w that terminating abruptly ē New Crops.

Pathogenesis of DH

(2011) Enhanced

- Pts with: Gluten sensitivity = Defective Mucosal barrier

- Gluten: Containing diet e.g Wheats → Passes to lamina propria of The Intestine.
  - ↓
  - Gliadin-TG2 Complex
  - ↓
  - Formation of Anti-TG2 IgA autoantibodies
  - ↓
  - Cross react with Epidermal TG3
  - ↓
  - Formation of IgA-TG3 Immun-Complexes
  - ↓
  - deposition in dermal papillae with Neutrophil chemotaxis.

Gliadin: is fraction of Gluten

TGs: enzymes in Tissues (TG2) use Gliadin as substrates

- Subepid. blisters (L.L)
- Neutrophil Microabscesses (IgA → ++ C3a → ++ Neut.).
- granular IgA deposits at dermal papillae.

Dapsone:	-- Neutrophil accumulation
Iodides:	++ " "

Dapsone is Rx of dis. of Neutrophils or IgA.

((NB))

يعني
بنشيل دابسون
ونكمل GFD
الدابسون نكمل
GFD

- GFD = Gluten - free diet
  - Dapsone نقطي تجعل نتحسن فترة ٥ بنشيل ع إشارة

- Sulfasalazine: Category (B) in pregnancy.
  - Dose : 1 - 2 gm/d
  - Sulfapyridine : 0.5 - 1.5 gm/d.

- S.E : Hypersensitivity
  - Hemolytic anemia
  - Proteinuria
  - Nausea & Vomiting الأهم

لازم يشرب كتير ماء لبنه

- Sulphapyridines:
  - Sulphasalazine
  - Sulphapyridine 1.5 - 4 gm.
  - Sulfamethoxypyridazine 0.5 - 1 gm /d

(تعاملية)
Intact bulla or Erythema

. Path: → subepid (intra L.L) blisters ē Neutrophilic infilt.
→ Neutrophil microabscesses (in) dermal papillae.

Eos. infilt is +ve So difficult to diff from BP ?? ↓ do (DIF)

أهم حاجة للتشخيص . DIF: → . 90 % (granular) Ig A in Papillary dermis. [hallmark] "مهم جدا"

(HL) . NB: Granular + lineare (5-10%) . Fibrillar : rare.

. IIF: Anti (IgA)
- . gliadin
- . TG (Transglutaminase) [antiendomysial]
- . Reticulin

. Targeted Ag: → Transglutaminase → Tissue: TG2 → Epid = TG3

(HA)

ممنوع أكل:
- . bread
- . Cakes
- . Salad,
- . Alcoholic beverages.

Stop gluten (Atkin diet)
- كل : O R C — oats (الشوفان) Rice Corn (ذرة صفراء)
- لا تأكل : Wheat, & Rye (القمح، الجاودار)
- Value:
  1. ↓ Cut & intest. manif.
  2. ↓ Dapsone or (Stop it)
  3. ↓ incid of Lymphoma.

↓ give

[Dapsone or Sulfapyridine]

(لو مفيش G6PD deficiency)
1. 100-200 mg/d (± ↑ upto 400/day) (أكثر تسبب هيموليسيس) (Hemolysis)
2. dramatic Response ē in 48 hrs. (Therapeutic Test — استجابة)
3. For 3-6 ms.

. 2-4 gm/d
. Sulfasalazine 1.5-4 gm/d (حلو) metabolized To → Sulfapyridine.

[لو مفيش دابسون و sulfapy.] ← Colchicine, Tetracycline, Nicotinamide, Ciclosporin (but ± → Lymphoma), Heparin ?

Cs → Systemic : No effect
→ Topical : ± ↓ itching

LAD = linear IgA Dermatosis (LABD = linear IgA Bullous D)

1- Classical lesions: Clear or Hgic roundish or oval vesicles & bullae on NL or Erythematous or urticarial skin

- Itchy
- Vesicles < Clear or Hgic
- Skin < NL / Erythe. / Urticaria
- MM
- Distribution
- Types of LAD
- Variants

- 50% ← Severe + early

• These vesicles & Bullae maybe arranged into 3 varieties.

- discrete (CBP like)
- Grouped (Herpetiform) (DH like)
- at Edge of annular or Poly Cyclic Erythematous or urticarial lesions. ✓

String of pearls or Beads sign

LAD & DH وجہ پشبہ بین

2- distribution & lesions

Adulthood LAD (≃ 52 Yrs)

- usually → Trunk & Limbs (→ lower)
- Rare → perineum & perioral

Childhood LAD (CBDC)

- start < 5 Y.
- Resolve: 13 Yrs (after 3-6 Yrs)
- usually → lower Abd., Anogenital & perineum
- others Face, perioral, Hands & Feet. (Acral)

3- other Non classical lesions:

- Erythematous ← Macules, papules, plaques
- EM-like (Targetoid)
- Morbilliform.
- Cicatricial Variant: EBA or CP like (& severe Mucosal effect)

LAD in children called chronic bullous dis. of childhood (CBDC)

NB: Skin lesions are itchy & have Burning sensat⁻ (but < DH).

MM affect⁻ (≃50%)
- Common & ± Early sign.
- has Cp like picture. (Severe)
- Any mucosal site ± affected.

Pathology: Early urticarial lesions:
- linear allignement of Neut. at BMZ.
- Neut. Microabscesses at dermal papillae (DH like).
- Vacular changes.

Path ج& DIF
DH: granular IgA & Neut. at dermal papillae
LAD: linear IgA & Neut at Very tip.

Late / vesicular lesions: intra L.L & ± SLD Blistering ē Neut. infilt. (± Eos.)

NB. Path → Non Specific (BP ≅ DH like)

(But) linear arrangement of Neut. along BMZ & Neut. at the (very tips) of dermal Papillae → Favors LABD > DH.

DIF: Linear IgA at
- L.L (Mainly)
- SLD (ass. ē Anchoring fibrils) (±)

± linear C3 & IgG

IIF: ≃ 50% IgA antibodies directed against:

(Ag)
- L.L ←
- LD -
- SLD -

- L.L antigens: • 97 KD, • 120 KD [Portions of Extra-cellular domain of BpAg2] or • 285 KD [Ag in L.L] (LAD 285)
- SLD antigen: → Anti Col 7 antibs. (Anti 250 KD protein Abs ā part from Col 7A).

Ladinin (in LD has role in Maint. of Form^n of Anch. Fibrils) — Other Ags
• BpAg 1

NB1: Conditions that may associate LABD:

- ulcerative Colitis (70%)
- Malignancy
- Drugs.
- Gluten sensitivity (GSE). (Rare)

NB2. Types of LABD: (4 Main types):

1. Idiopathic (Classical) Type: 2 Age peaks
   - preschool (5ys)
   - 60 ys.

2. Drug induced: (جديد برضينا)

   2 ch:
   - No MM
   - resolve after stop of drugs.

   - Most Common: Vancomycin (مهم قوي)
   - less Common: ACEI, NSAIDs, penicillin, & Cephalosporins, "diclofenac"
   - uncommon: phenytoin & Sulfa.
   - rare: Ciclosporin, PUVA, Rifamp.

3. Malignant associated.
4. GIT disorders ass: GSE & U. Colitis.

- Prognosis of LABD: in Majority of cases; resolve after 3-6 ys.
  (نسبة شفاء كاملة [10-15% in 30-60%])

Treatment

أهم علاجين

1. Dapsone: (الأهم) → dramatic c in 2-3 ds.
   - children: 1 mg/kg/d
   - Adult: 100-150 mg/d.
2. Sulphapyridine: (بديل للدابسون)
   - 250 mg - 1.5 gm.

- Others:
  1. Cs (systemic)
     ممكن نحتاج نضيفه للدابسون عشان نغطي سيتنج أفضل
     - usually Needed for pt. c IgA & IgG deposit.
  2. others (مهم)
     - Tetracycline / dicloxacillin & Erythromycin
     - other Immunosupp.

EBA (Epidermolysis Bullosa Acquisita) (4-1)

خالص
دارسوس

- 40-50
- Ass.

HLDR2

- Age: Any but more in elderly (40-50)
- M>F
- Ass.
  - DM (dermatomyositis)
  - SLE
  - lymphoma
  - Myeloma
  - Amyloidosis
  - IBD

(HLCTD) (MG) (IBD)

(نزنن)

Clinically

Generalized Inflamm. type (non-scarring)

↓

B.P (Dermolytic P.) like.

or

CP

↓

wide spread tense bullae → No scarring

↓

(H) (good prog. / responsive)

1. Cs
2. Dapsone
3. Immune supp.
4. IVIG

Localized non inflammatory type (Commonest)

↓

DEB or PCT like [So called Acquired Mechanobullous]

↓

- Skin: Traumatic blisters → (Fragility) scar, Hyperpigm. & Milia. (Acral & Trauma sites) elbows, knees, dorsal Hand & Feet.
- Hair → scarring Alopecia.
- Nail → dystrophy
- MM → usually affected.

↓ (H) [prolonged / resistant to H]

1. avoid Trauma
2. wound manage
3. # inf

Path.

Histopath

Subepid (Sub LD) or ± L.L Blister.

- Neutrophil ↓ inflamm. type
- non inflamm. type ↓ Absent or sparse infilt.

DIF (100%)

↓ مثل

B.P

↓

linear IgG (+++) > & C3 (+) (SLD) diagnostic

Expl. DD < BSLE, BP.

IIF (50%)

- Anti BMZ Abs directed against Collag. 7 & Anchoring Fibrils in Sub. LD (IgG only)

##of EBA

(Very chr. dis & very resistant to ##)

- No universally accepted ## d.t lack of studies & rare cases.

- Best ## b/ some authors:
  - Steroid + Dapsone or Sulphonamides.
  - Colchicine
- Other lines:
  - Pulse Cs
  - AZath.
  - MTX
  - Vit. E & C
  - Ciclosporin
  - IVIG
  - Plasmapheresis

Bullous SLE

- IgG & IgA against Coll 7
- during exacerbat° (WLE)

- Def. Transient autoimmune blistering condition that occurs in the setting of SLE (1% of cases)
- NB: there is some controversy as to whether the term include all bullous erupt° ē SLE or should be reserved for those ē derma Ag. [Coll 7].
- CIP / Tyffes / Criteria for Ø (see CTDs)
- Histopathology "Lever" 3 Histologic pattern:

Subepid. Blistering ē Dermal Neut. Microabscesses

1. DH like → Most Common.
2. Basal cell layer Vacuolizat° ē subsequent blistering
3. Vasculitis ē subepid blister & Pustule format°.

(to diff. from DH: . Mucin deposit° (amone / Collagen)
. Thickening of BMZ.

BSLE

(عشان کده عالجی Dapsone)

1. ~~Def~~
2. CIP → B.P or (DH) like (ex. at sunexposed + SLE picture)
   "Generalized Ep. at sunexposed"
3. Pathology, DIF & IIF → as EBA
4. Steriod, Dapsone, MTX or Rituximab.

(N لاحظ) So How to diff.

- **EBA**
  - Trauma site
  - Skin fragility
  - Heal c scarr.
  - IgG only

- **BSLE**
  - sunexposed areas (mainly)
  - Hx & manif of SLE
  - dramatic Resp. (+ve) dapsone.
  - IgG & IgA.

خلي بالك 2 diseases c dramatic Response to Dapsone ?? → DH & BSLE (also LAD)

EBA & B.P (عايزين نفرق)

- Blister → B.P L.L. / → EBA SLD.
- infilt → Eosin. / → Neut.
- C3 → : B.P > IgG (while) EBA عكسها
- ~~IIF for~~ Salt split skin
  - BP: epid. side.
  - EBA: dermal side
- Skin Biopsy & Immunohistoch
  - Collagen 7 Abs < BP: at base of blister / EBA: " Roof. "
- DIF: EBA → U serrated pattern / BP linear.

- EBA & BSLE → (الخلاصة)
- BSLE → Clinically as → (DH or B.P) / → Immunologically → EBA.

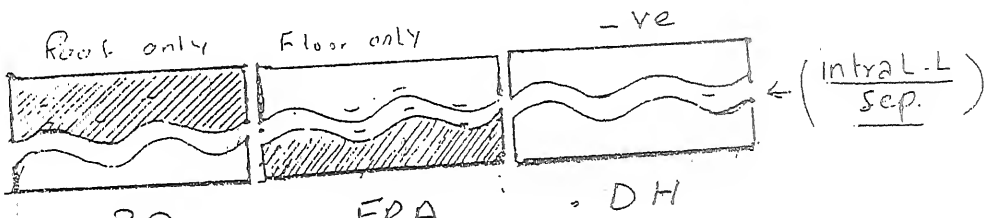
1- split skin technique.

(اختبار واحد لكل Subepid.)

expansion of DEJ through (L.L) by osmotic exposure to hypertonic 1 molar NaCl for 1-2 days at 4°C, (IS) essential for IF evaluation of subepid bullous dis.

(NaCl 4°C)

• Can be done for both DIF & IIF., the later the auto Abs will reach the epid. & dermal side of skin.



- BP
- CP
- HG
- LABD (Majority)

(anti BP Ag2)

- EBA
- BSLE
- BP (anti-P 105 ؟)
- CP (anti laminin CP)
- LABD (minority)

Dapsone in Subepid. Blistering dis.

- localized CP
- DH
- LABD
- EBA
- BSLE
- SCPD

Non Auto Immune Bullous diseases

Subcorneal pustular dermatosis (Sneddon & Wilkinson, 1956)

It is a chronic benign relapsing pustular eruption which affects mainly the trunk, spares the face and mucous membranes and histologically shows subcorneal bulla which contains polymorphonuclear leukocytes.

- Age: 40 - 50 ys., Sex: more in female (4:1).
- **Clinically:** Chronic relapsing disorder, with sterile pustules in annular or serpiginous patterns mainly on the abdomen, axillae, and groins. Pus accumulates in the lower half of large pustule (level). Healing occurs with superficial crust and later on with brown pigmentation. The face is never affected nor the mucous membranes.
- **Associations:** IgA monoclonal gammopathy, pyoderma gangrenosum, inf. bowel dis.
- **Histopathologically:** Subcorneal neutrophils. Later, few 2ry acantholytic cells are seen at the base of a pustule (probably due to proteolytic enzymes present in the pustular content). Dilated capillaries and perivascular mainly neutrophilic infiltrate are present in the underlying dermis.

  Some authors believe that subcorneal pustular dermatosis is a variant of pustular psoriasis, however, spongiform pustules occur only in pustular psoriasis.
- **Treatment:** Dapsone 50-150 mg daily or sulfapyridine.

Subcorneal or intracorneal separation with:

Neutrophils predominant	Eosinophils predominant	No or few inflammatory cells
• Impetigo contagiosa	• Erythema toxicum neonatorum	• SSS syndrome
• Pustular psoriasis		• Bullous impetigo
• Subcorneal pust. dermatosis		• Pemphigus fol.
• IgA pemphigus (SPD type)		• Pemphigus erythem.
• Candidiasis	• Eosinoph. pust. folliculitis	• Miliaria crystallina

- IF → -ve but recently IC IgA in epid.

- NB:

SCPD like dis

- pustular Ps.
- SCPD like IgA Pemphigus.
- Amicrobial pustulosis of the folds
- Pyoderma Vegetans.

(1939) [Arabic] ← . Hailey - Hailey (By Familial ch. pemphigus) (53)
(Darrier أخوال)
(EMed 2ch) Darrent

. Inheritance

. AD
. + FH → (60 ?)

. Age : 30-40 ys.
. Pathophysiology : < Genetic + others

[ATP2C1 / hSPCA1 → desmosomal defect → Blisters.
(Ca+ Pump protein)

. defect on gene called (ATP2C1) Found on (Golgi) Chromosome 3q21-24 —Codes For→ protein hSPCA1 (PMR-1) w̄ is Ca+ & Mn. pump → defective desmosomes (depend on Ca+) → separat.

↙ مثل Darrier

. Other Factors share in the dis.
- Heat, Frict., Inf (Bact & yeast)
- UVB : provokes acantholysis (& used to detect Gene Carriers of the dis.)

. ultrastructural studies: KCs show:
- retracted tonofilaments
- Elongated memb. microvilli
- ↓ No of desmosomes.

. C/P : → Flaccid vesicules/pustules: < crusted lesions. / circinate ~ . / vegetating ~ .
- that rupture → Crusted lesions or
- Form expanding Circinate plaques c̄ central healing → Pigmentat. or
- Form moist, Malodorous flat soft vegetat. c̄ painful Fissures & (2ry Inf.)

Site ↓ Flexures (one site or Multiple sites)

. Pain, burning & itching → limit the mobility of Flexures.

. other ass. cut. lesions: < PP pits / Nail bands, white. —مثل→ Darrier. / Mucosal: rare oral (buccal) ± vaginal or Esoph.

. Complications: [1- Eczema Herpeticum (عدوى)
2. ACD
3. Malignant transformation → SCC (تاصّيف ?)

. prognosis: [. Exacerbat^ usually at warm seasons.
. improvement ± occur in old ages.

. Pathology: حاجتين مهمين < Dyskeratosis (±), Acantholysis: (++ +):

↓ Early
[. dissolat^ of: APs
. Tonofilament Separat^ → aggreg. around Nuc. → Dyskeratosis

Suprabasal Acantholysis (widespread)
. Extensive but < PV
→ Few bridges (desmosomes) remains → Dilapidated brickwall

Villi inside the Blister Cavity.
(Elongated dermal Papillae) & a single layer of Basal Cells lines the Villi.

. ultrastructure: → as before"

. IF: → ??

. Treatment [Course waxes & wanes].

1- Topical: (Astringent Agent).
. Soothing Compresses: Alum. Acetate (1:40) dilut^
Alum. Chl. 20% in Alcohol
. Topical Cs
. Topical Antib. & Antifungals.
. Diavonex (Control Ca+).

2. Systemic:
. Antibiotics (tetracycline & Erythromycin) → ↓ protease Activat^
. Cs (↓ Acantholysis).
. MTX
. Retinoids (Few reports) +ve Emed. [ ]
. PUVA (±)

3 Recent
. BOTOX → ↓ hyperhidrosis.

4 Grenz Zone Therapy ..

5. Surgical: dermabrasion + CO2 laser, Cryo

(EMd 2009)

Acantholytic Dermatosis (AD)

often persistent & resistant to tt so the PAD ←
- Transient AD (TAD → Grover's dis (1970)
- Persistent AD (PAD → 1976).

صورة:
- ♂ > 50 ys.
- Exacerbat : Summer, Sweating, Sun light, Heat & Fever
- lesion : discrete papules or papulovesicles.
- Site : central back & chest, Neck, lower part of rib cage
- Itching (..chic ...)
- Course < Transient : ws – ms; persistent : Several ys.
- Ass. [AD. CD.] [X. Eczema, Cancer Skin.]
- Histopath. : 5 Histological patterns :-
  - PV like.
  - PF like.
  - Darier like.
  - HH like.
  - Spongiotic dermatitis like.

Focal Acantholysis + Dyskeratosis + Spongiosis

Aphthae like oral lesions ± occurs.

Pathogenesis :
- small molecules seep through sweat duct → Acantholysis
- mild thermal injury → enzymes → Acantholysis
- M. Furfur
- Demodex

. IF → – ve (ddx non Immune Bullous)

℞ :
- Topical : Potent Cs, Menthol lot
- Systemic : VitA, Isotretinoin, Cs. PUVA, MTX

ok.

• EBS (Epidermolytic = Intraepid Blistering)

(الحفظ خصائص العامة)

1. All AD Except < Muscular dystrophy Type (AR). / Some Cases of Koebner (AR)

2. All dating since birth or Infancy Except Weber-Cockayne.

3. All d.t defect of K5 & K14 (KIF) Except: (Plectin, Integrin)
   - Muscular dyst. → (Plectin)
   - Mottled Pigm. Type → K5 only
   - AR Koebner Type → K14
   - EBS Superficialis → Coll. 7 ?? & plectin.
   - Ogna & Pyloric Atresia → (Integrin) ??

4. All without → scarring, milia, MM, Nails, Teeth & hair
   Except → Dowling (Scar, milia, MM, nail) &
   → Musc. dystrophy (MS)

(نادرة) Other Rare EBS
1. EBS superficialis
2. lethal Acantholytic
3. Plakophilin 1 deficient
4. AR

• Types (WKODW)

• W • K • O • D • W with < Mottled Pigm. / Musc. dystrophy (نادر)

W → Weber-Cockayne (localized Type)
- Palmoplantar only
- at Childhood

طفل أو شاب بيجيله باستمرار فقاقيع مع المجهود والمشي الكتير

K → Koebner (Generalized)
- AD ≫ AR
- Generalized
- (Sp) at large joints in Infant & child: occiput, back, Leg & large joints, also pp.

O → Ogna (Bruising)
- Hgic bullae
- Easy Bruising
- Nail onychogryphosis.
- ↓ (CRBCs enz Glutamic Pyruvic Transaminase).

D → Dowling-Meara ("Herpetiform")
- grouped or Herpetiform in Polycyclic or Annular pattern.
- PPK
- Scar, Milia, Mucosal & Nail aff.

• Most Common Types	• Most Severe
Weber, Koebner, Dowling	Dowling (Herpetiform)

JEB (Atrophic EB)

(Blistering at Level of L.L).

(Sheet)

1. All AR dating since birth.
2. All d.t defect in Laminin 5 → Genes: LAMA3, LAMB3, LAMC2
   - Except:
     - GABEB → BpAg2 (± laminin 5)
     - JEB ē pyloric atresia → α6, B4 integrin.
3. All show:
   - Atrophy & scar.
   - Hair
   - Nail
   - MM
   - Teeth (dysplasia)
   - + (Except) "Gravis" minimal scarring & milia.

Teeth → Atrophy; Teeth dysp (Enamel) نقل الإنزاع (pitted teeth)

الأنواع
- Herlitz (lethal) → 2 Extract. → أول ما تتوقع (مولود) → "Ensure Air way"
- Non Herlitz (non lethal) باقي الأنواع
  - mitis
  - nH-PA
  - GABEB
  - localized
  - Cic.

A. Gravis (Herlitz = Lethal)

1. Systemic & Mucosal affect:
   - anemia
   - GR
   - GIT affect
   - Corneal affect
   - laryngeal → Hoarsness → RD, Death (Elect. imb. & inf.) → Omnious sign at birth

2. Cut. Manif.: Generalized blistering ē Marked Facial Erosions & chic peri oral, peri-nasal & perianal Exuberant G.T. (أول حرفين → Death)

2. No (مش بيعمل / لا يمين):
   - Hand affect
   - Scarring (بس غالباً بيموت)
   - milia

Most Common: Herlitz, GABEB

B. Mitis as Gravis Except:
- No Systemic
- No GT.
- Non Fetal
- (Good prognosis)

C. With pyloric Atresia ass ē ...

D. GABEB as Herlitz except:
- Atrophy (no scarring)
- Non Fatal
- Bald, Atrophic scalp
- ± SCC.

Non Herlitz ← الاسم الجديد

(E) Inversa: Flexures

(F) Cicatricial: Scarring → Syndactyly & ant. Nasal Stricture

(G) Late onset: at PP, Elbow, Knee
: Deafness & loss of Finger print.

(H) LOC Synd

DEB (Dermolytic)

(Separation at level of SLD)

d.t defective Collagen 7

AR (RDEB) =

- Hallopeau S.
- Others:
  - mild Generalized
  - Inversa
  - Prurigihosa
  - Centripetalis
  - BDN (ARIAD).

4 Ch:
- Poor prognosis.
- More Severe
- Acral deformity
- Extracut. manifs.

AD (DDEB)

4 Ch:
- good prog.
- less severe
- No Acral deformity
- No Extrac

NB: RDEB:
- Hallopeau Siemens (HS) [Mutilating]
- Non H-S:
  - mixed non mutilating Type
  - Inverse.
  - Centripetalis.

6 Types:
- Generalized
- Acral
- pretibial
- Prurigimesa
- BDN
- Nails only.

(1) Hallopeau Siemens (Gravis)

(Skin + systemic)

- Generalized scarring
- Others: Milia, Alopecia, M/M, Nail, Teeth (Severe dental caries)
- Anemia
- GR → (Clinic) club like Feet or mitten like deformity (gor at 25 Y)
- Oesoph. stricture
- Systemic Amyloidosis (Fatal)
- ↑ Risk of SCC (age)
- Osteoporosis

(Pseudo Syndactyly)

(Fusion of Fingers & digits → resorption of bone & muscle. Atrophy)

(Non H-S RDEB)

- Mild Generalized: less severe than H-S
- Inversa: at Flexures
- Centripetalis: Slow progressing From Acral → Trunk.

AD DEB (DDEB)

1. Cockayne Touraine
2. Pasini
3. Pretibial DEB
4. EB pruriginosa (AD > AR)
5. Barts Synd
6. Bullous dermolysis of the new born (AD/AR)

(Transient) (TBDN) → 5, 6

---

(1) Cockyne - Touraine (Classical DEB):

- less Cut. Fragility than RDEB → Sharp Knocks or Blows are need to induce bullae rather than mild Fric.
- Skin: Acral blistering (Elbows, Knee, dorsal Hand & feet) → localized scarring & Milia.
- MM → NL & NL Teeth. (Atrophic or Hyper.)
- Nails: dystrophic (very chic as many PT has mild scarring)

(2) Pasini = Albopapuloid: as Cockayne but:

- More severe (± & Nikolsky's sign).
- Albopapuloid scars: Spontaneous, Flesh Colored, Ivory White perifollicular scar like papular lesions on Trunk (Sp. Lumbosacral).

(3) Pretibial DEB: itching, bullae, Atrophy & Scaring at Shin

(4.) EB pruriginosa:

- Severe itching
- Mild Acral Blistering
- linear, Vicfaceus papular & nodular lesions at shins & forearm.
- Nail dystrophy

(5.) Barts Synd.:

- Skin Fragility + "Cong. localized Absence of Skin at lower legs."
- Ass. Features: Cong. L.L Anomalies, Renal Aplasia & Mandibulofacial distasis.

(4.) Bullous Dermolysis of ! New.born (Transient BDN)

vesicular ullous Eruption at birth that's induced by Friction resolves spont. at 4 mo's without scarring.

Mixed EB = Kindler synd [AR].
(Acrokeratotic poikiloderma)

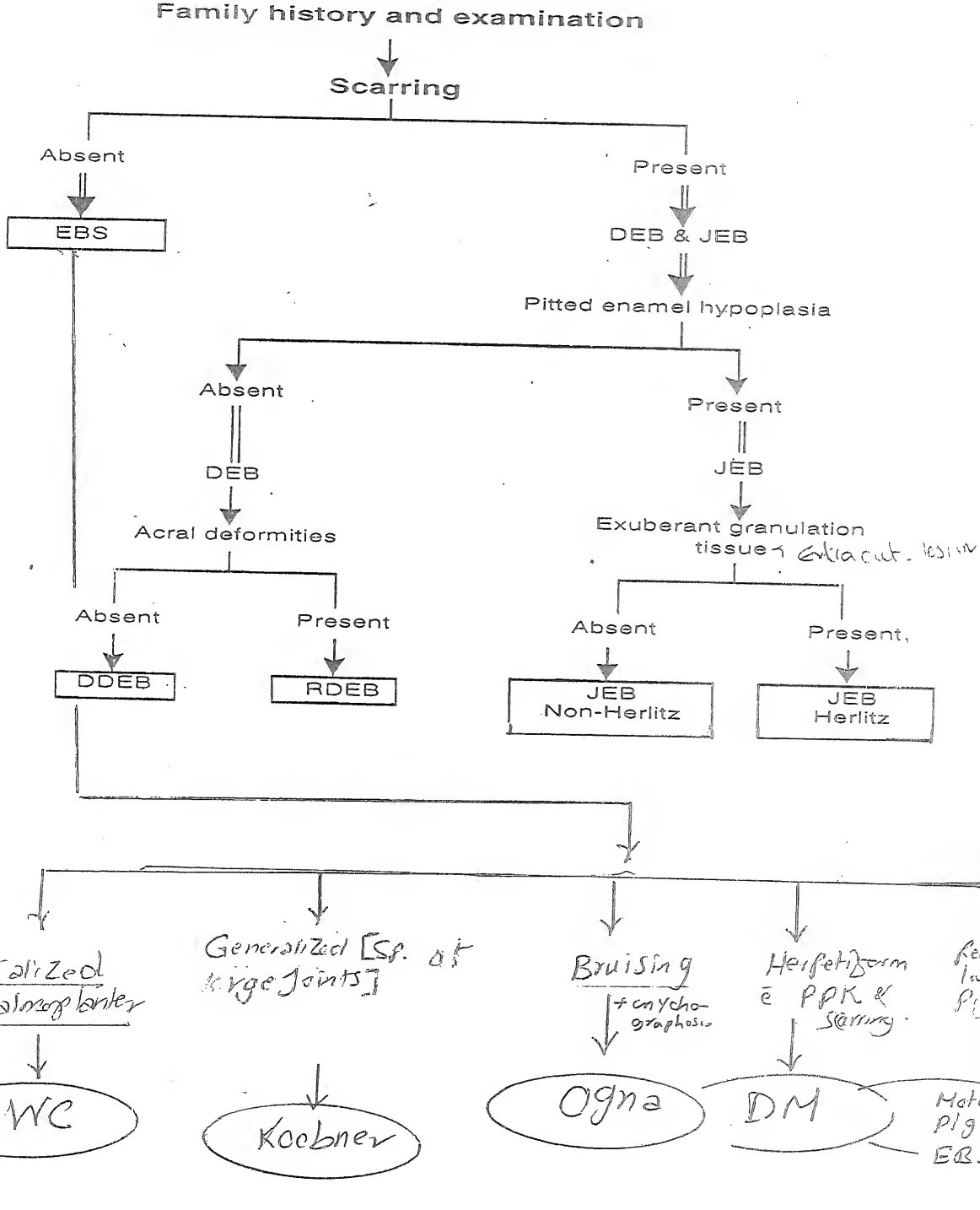
- Generalized Poikiloderma
- Photosensitivity
- Acral Blisters. (PD)
- Acral Keratoses
- Pseudoainhum.
- Gingival Affection

Diagnosis of EB

A. Clinical : Hx & Exam

B. Lab. - Biopsy
- EM
- Ag Mapping
- Antibody using [Immuno-histochemistry]
- Molecular diagnosis.

A. Clinical Diagnosis



(WKODW)

Lab. Diagnosis

1. Skin Biopsy: to determine level of Blistering.

2. Transmission E/M:

determine 2

- Blister level
- Evaluation of Basal KCs: Tonofilaments, HD & Fibrils

EBS → Basilar (Intraepid) ↓ Just above HD & CM.

JEB → Intra L.L

DEB → SLD

EBSS → Subcorneal.

EB subtype	Ultrastructural findings
EBS	Clumped tonofilaments in EBS "Dowling-Meara" (NL WB)
JEB	Absence or markedly reduced numbers of hemidesmosomes
DDEB	Reduced number of anchoring fibrils
RDEB	Absent or markedly reduced numbers of anchoring fibrils

Pathognomonic.

3. Antigen mapping:

. Immuno histo chemical staining of DEJ

By using Antibodies against:

Split-Skin Test

- K5 & 14 → stain Basal KCs
- BPAg1 (320 KD) → stain lower surface of Basal KC
- Laminin 1 → stain LL & LD
- Type VII Collagen → SLD

Fluorescent labelled Abs: [Blister بالنسبة للـ]

EBS: all Abs stain Base of Blister Except Anti K5 & 14 stain the roof & Floor

JEB
- Anti Keratin & Anti BPAg1 → Roof
- Anti Coll (7) → Floor
- Anti laminin 1 → roof & Floor.

DEB: All Abs Stain Roof only.

4 Immunohisto Chemistry ; For detection of ↓ or Absent Ag. Expression:

By using monoclonal Abs → ↓↓ staining of Targeted Antigens in Each Type of EB (... مش كويس!)

5 Molecular Diagn.: ↓ Abs: < 19 DEJ-1 → -ve staining in all JEB
LH7.2 → " " " RDEB.

Mutational Analysis. (مش كويس) AR

6 Collagenase: → ↑↑ (in) RDEB

↑ degradat of Coll < I III VII

Treatment — No Specific therapy.
No Effective "
Based only on avoidance of Trauma Fric

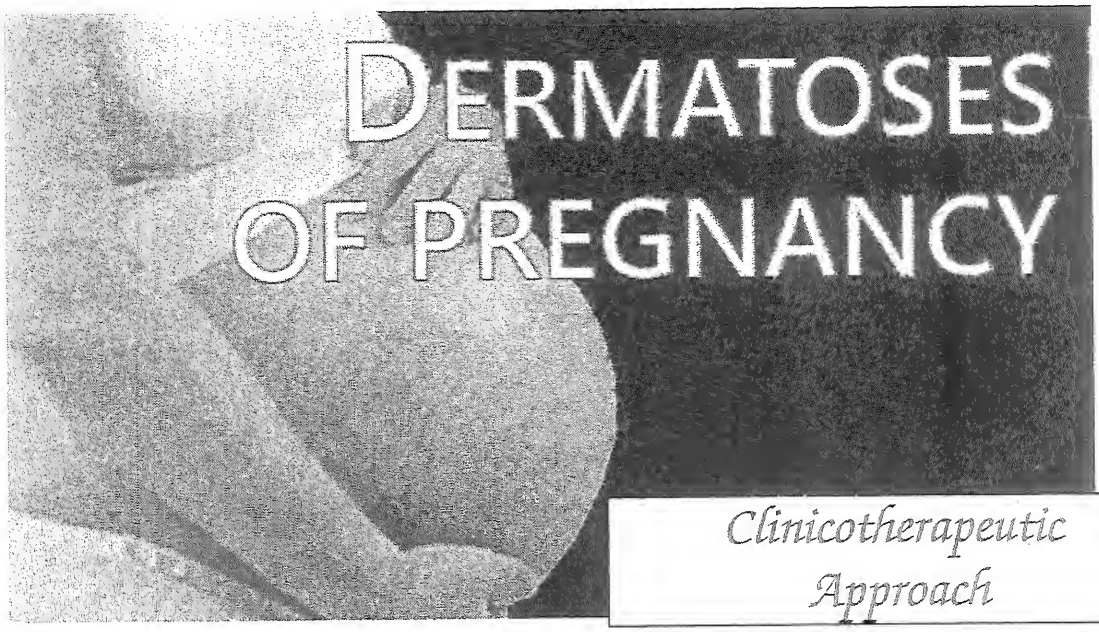
Treatment

1. Fetoscopy and prenatal biopsy at 18-20 weeks gestation for electron microscopic examinations to show any defects of basal keratinocytes, tonofilaments, hemidesmosomes, anchoring filaments or fibrils.
2. Prevention or control of friction or trauma with nutritional supplements. < Vit Zinc — why? to prev. Stricture.
3. Topical antibiotics.
4. Vit. E orally.
5. Phenytoin in RDEB: not effective. (Mechanism → -- Collagenase). (غير فعال)
6. Systemic steroids.
7. Surgical intervention to correct disfigurement.
8. Minocycline, cyclosporin, retinoic acid, gene therapy.

9. Gene therapy: [Future]

AR DEB
- Introduct of NL Genes into Nucleus of epid. Stem Cells
↓
Formation of NL proteins.
- disadv. Gene is degraded, Neutralized by Abs or shed insid a differentiating KCs.

AD-DEB
↓
Inactivat of Mutant Genes.
بدل ما ينزل جسم طبيعي هانزقه عمل الجسم الغير طبيعي



DERMATOSES OF PREGNANCY

Clinicotherapeutic Approach

Dr.Hany Abo Al-Wafa, MD

Definition

Cutaneous changes secondary to pregnancy related hormones as:

- **Estrogen**
- **Progesteron**
- **HCG &**
- **↑↑levels of Pituitary, Thyroid & Aadrenal glands Hormones**

Pathogenesis..
Basic Immunology

Types Of WBCs

Granular

(Cytoplasmic Grs. &segmented Nucleus, NEB)

- Neutrophils
- Eosinophils
- Basophils

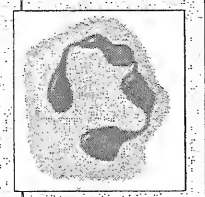
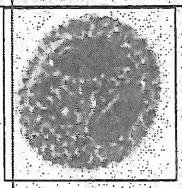
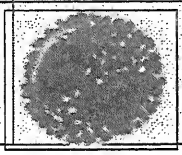
Non Granular

(Neither Granules Nor Nuclear Segmentation)

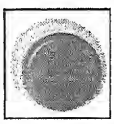
- Monocytes
- Lymphocytes

(Mononuclear Cells)

Granular Leukocytes

Type% of total WBCs	Diagram	Nucleus	Granules	Main targets
Neutrophil (62%)		Multilobed	Faint Pink.	- Phagocytosis and - Degranulation→Antimicrobial peptides (Myeloperoxidase, , defensins, cathelicidin, Alkaline phosphatase, collagenase, lactoferrin and cathelicidin)
Eosinophils (2.5%)		Bilobed	Pink	- Degranulation→ proteins (ECP, MBP, Cytokines, GFs) → attack parasites & Modulate allergic inflammatory responses
Basophils (0.5%)		Bi or Tri-lobed	Blue	-Release histamine, Heparine → role in parasitic infestation and Allergic diseases

Non-Granular Leukocytes (Mononuclear Cells)



Lymphocytes

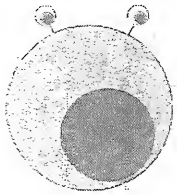
Monocytes

T-Lymphocytes

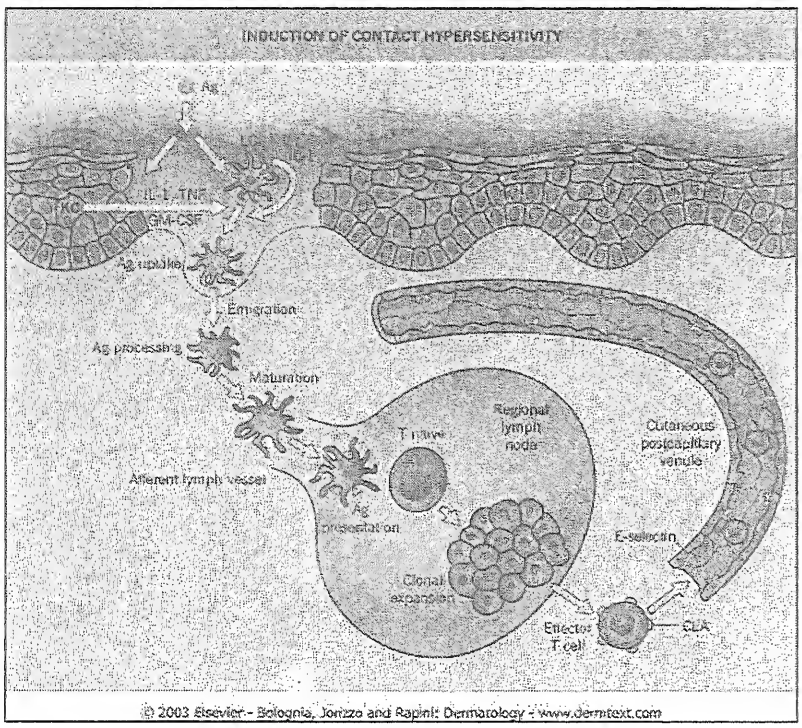
- Naïve (T0)
- Helper (CD4)
- Cytotoxic (CD8+)
- Others *(Memory, NKT, Mucosal associated&γδ T cells)*

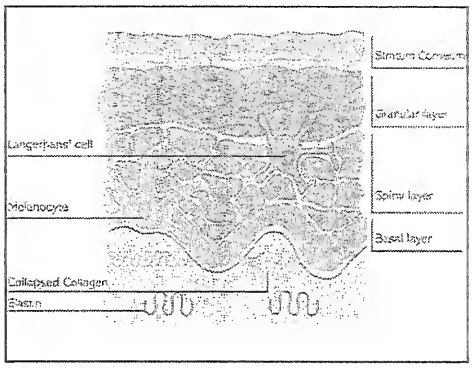
B-Lymphocytes

Plasma Cells



Langerhan's Cells+NaïveTC → TC differentiation



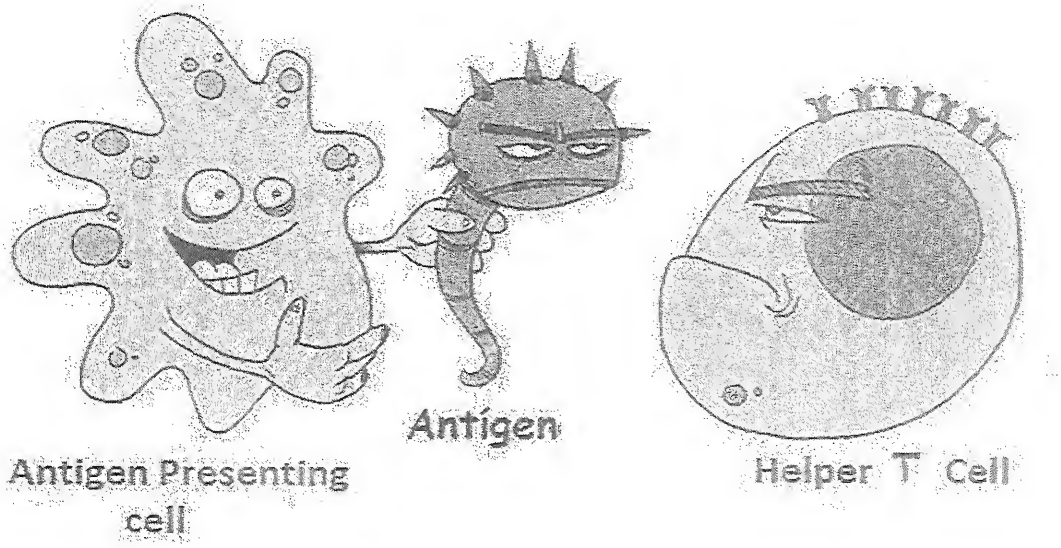


APCs+Naïve T cells (T0)

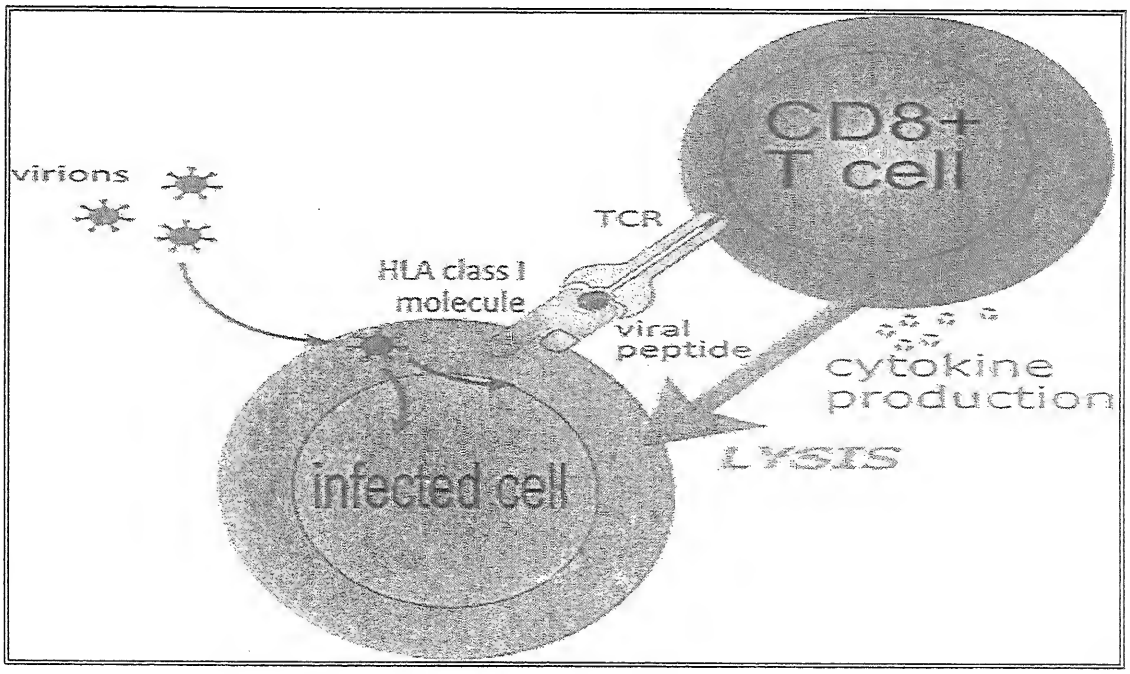
- T-Helper (CD4, Th0)
- Cytotoxic (CD8)
- Others: Treg, Memory, NK

- **Th1**
- **Th2**
- **Th17**

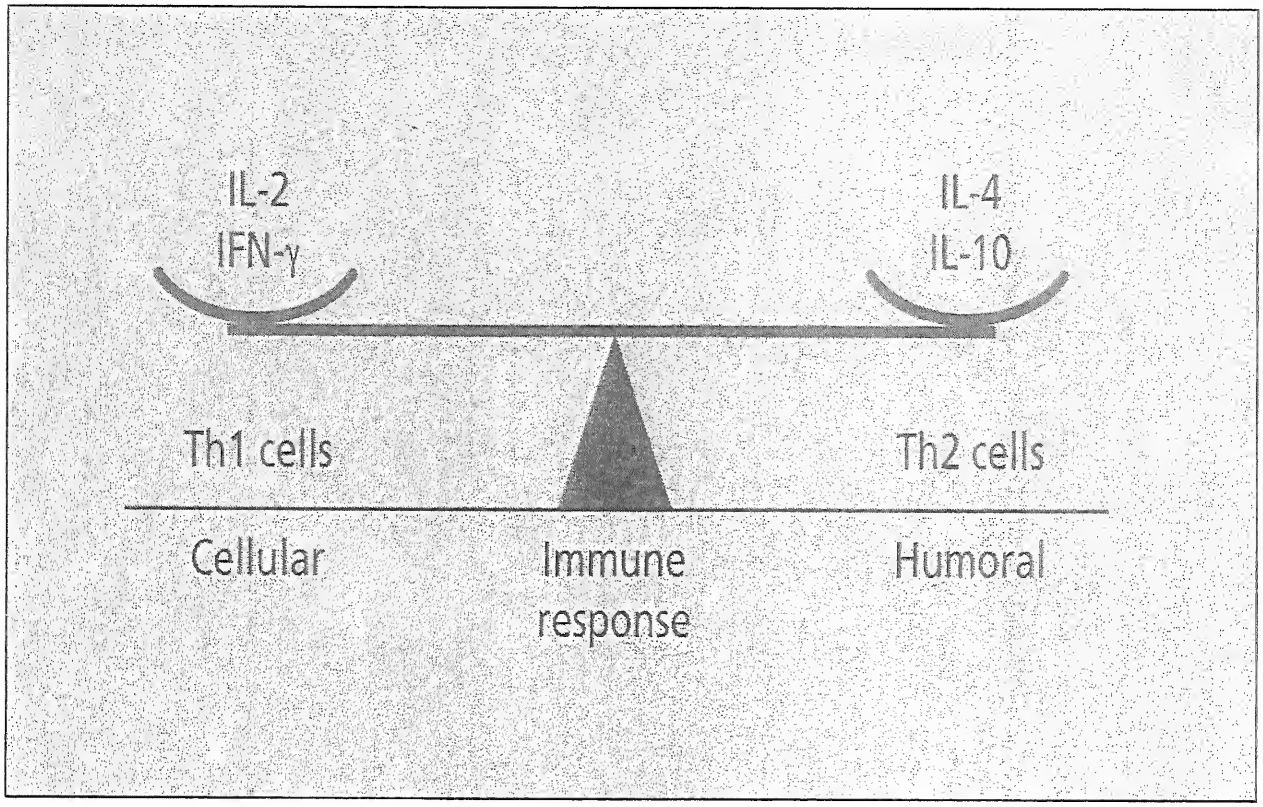
Interaction Between APCs &NaïveTC



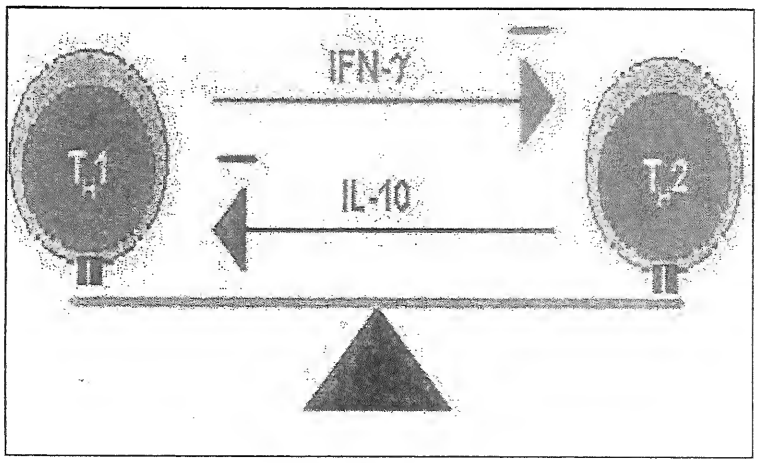
CD8+ interact with non Professional APCs (virally infected and Tm cells) which express antigens on their MHC-I

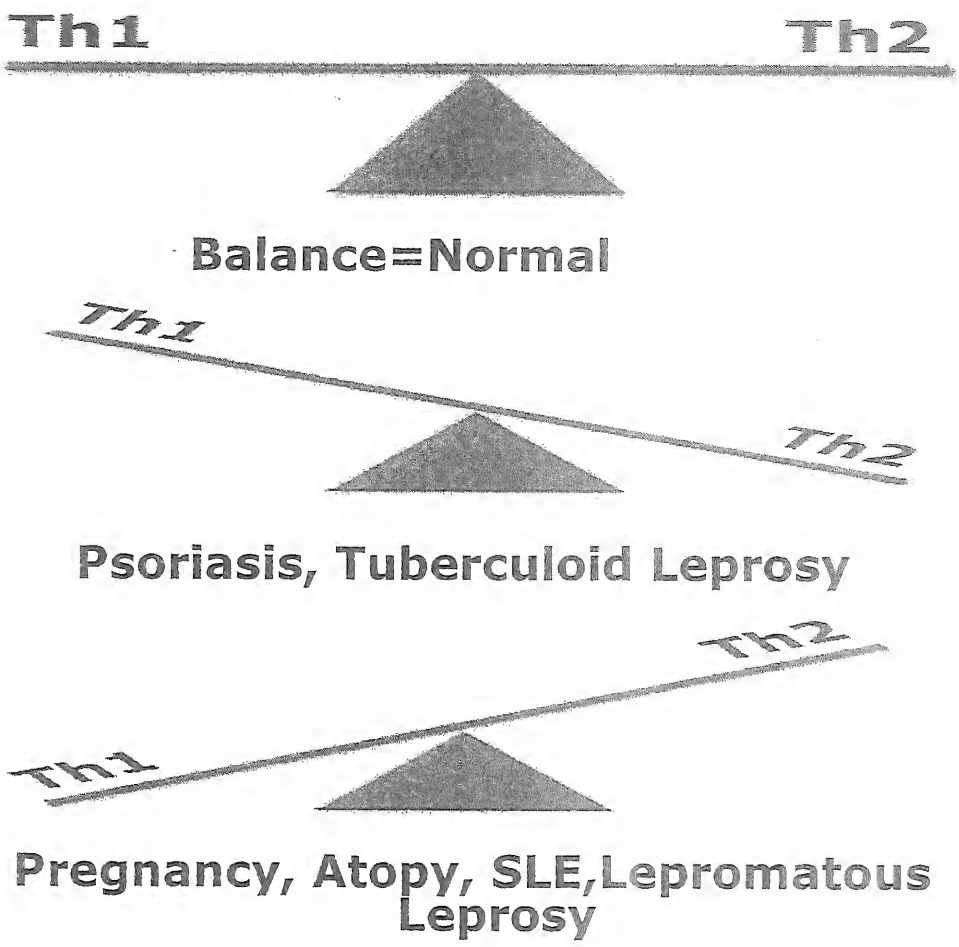


Th1 *Vs* Th2



Th1 &Th2 Conflict





Classification of Dermatoses of Pregnancy

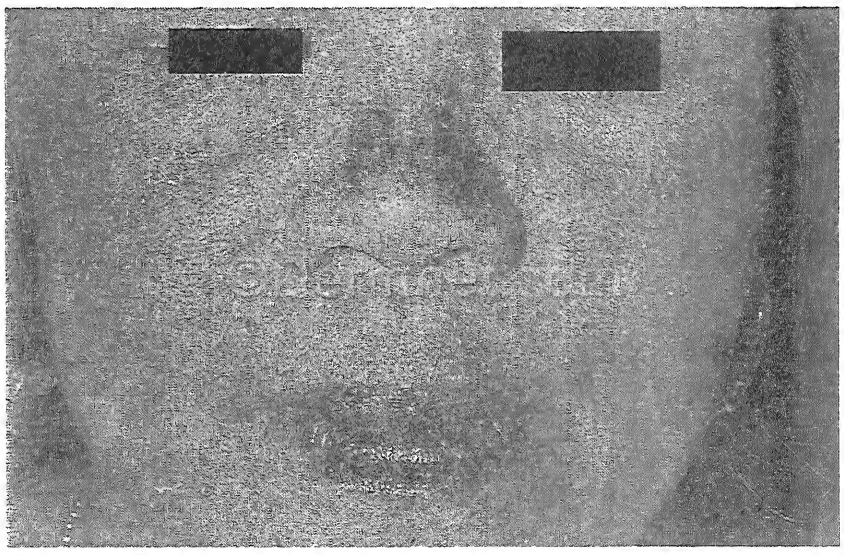
- Physiological changes during pregnancy
- Dermatoses Exacerbated or Improved during Pregnancy
- Specific Dermatoses of Pregnancy

I- Physiological Changes during Pregnancy

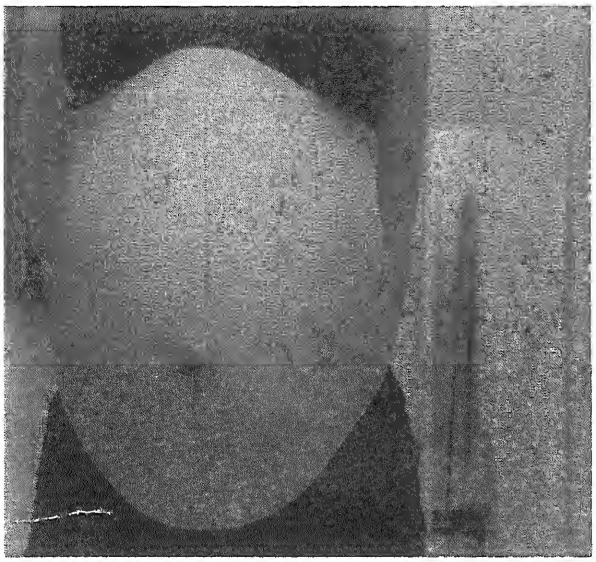
- Most of them are spontaneous and may resolve after pregnancy

Hyperpigmentation

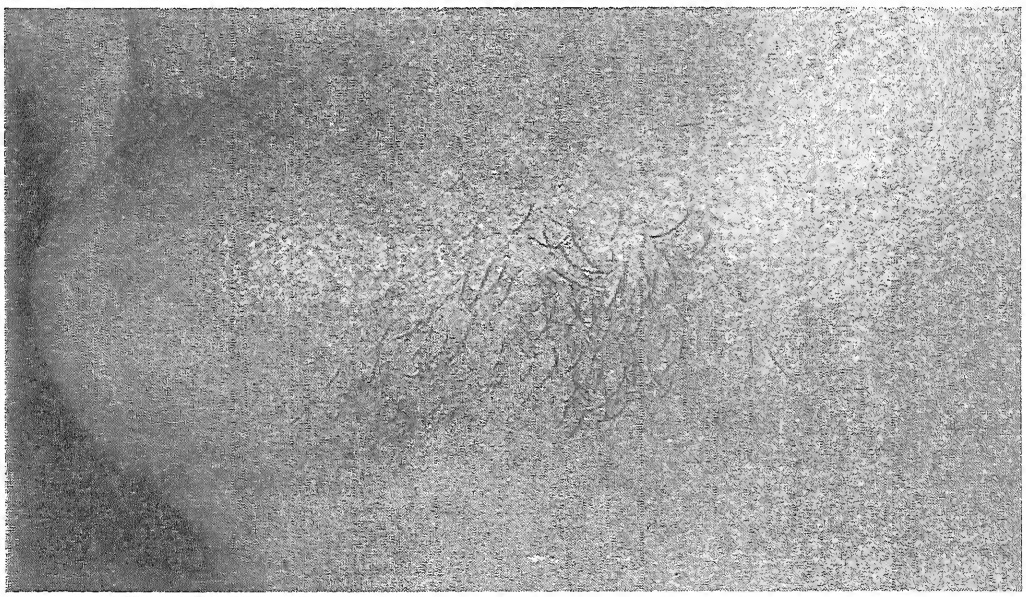
Melasma (chloasma)



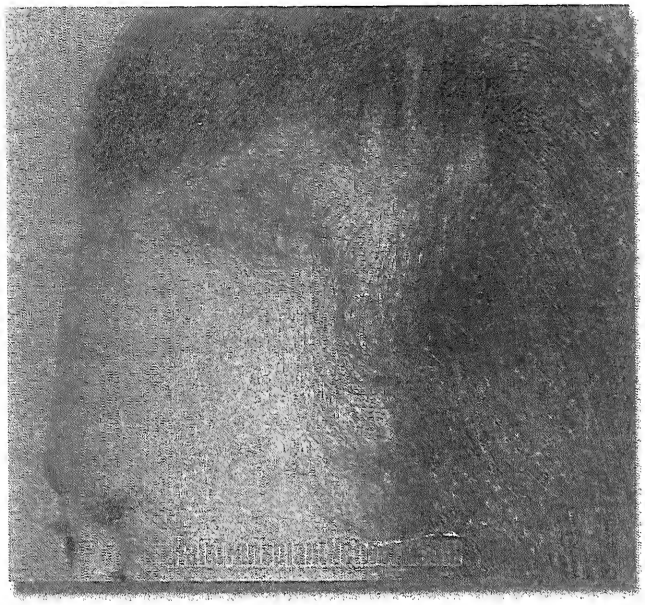
Linea nigra and Flexural Hyperpigmentation



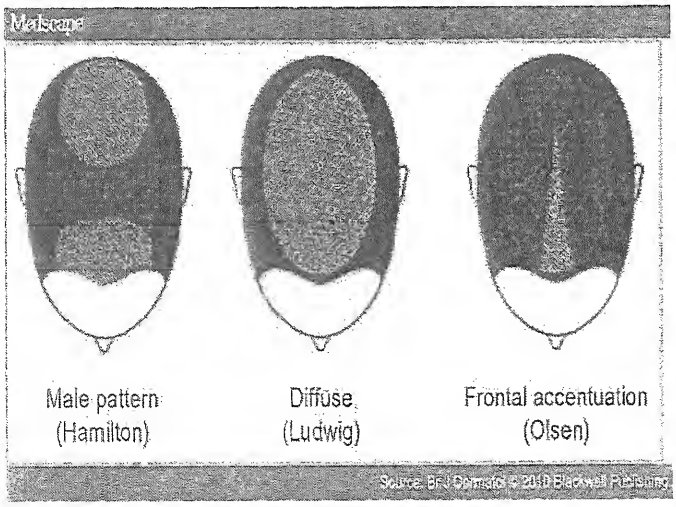
Hirsutism

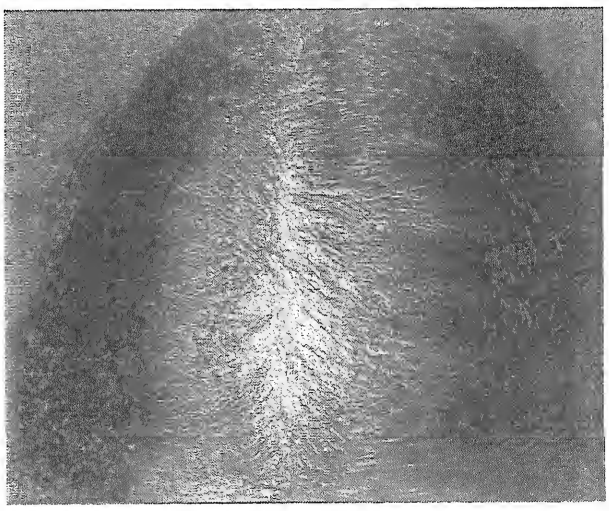


Postpartum Telogen Effluvium

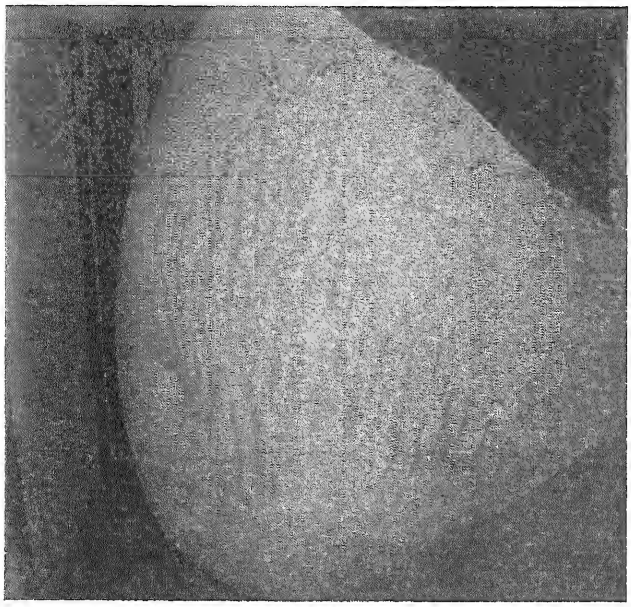


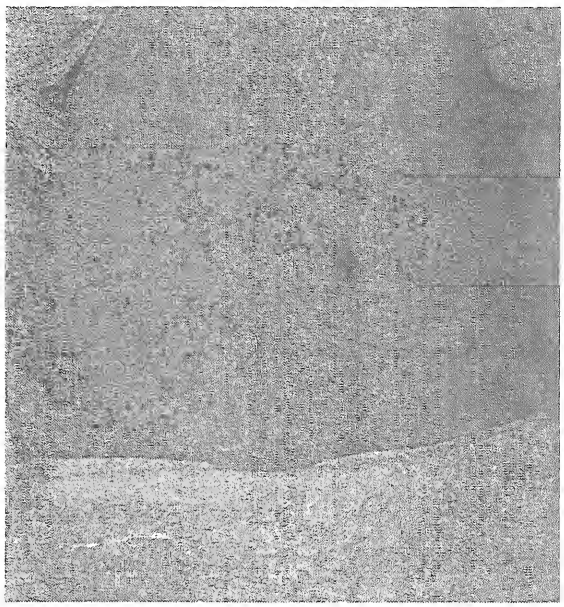
NB: AGA Shows preservation of anterior Hair Lines





Striae Rubra/Alba





Treatment of striae, an evidence based *(BJD, 2014)*

I- General Rules

- There is neither accepted nor ideal modality
- Striae rubra are resposnsive to therapy while alba rarely responding
- There is no prophylctic TTT for pregnancy associated striae, while Avoidance of rapid weight loss or gain may help prevent puberty and obesity associated striae

II- Medical TTT

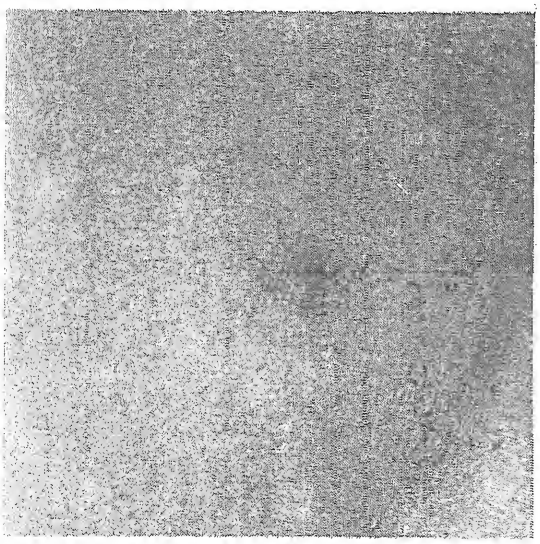
Topical Retinoids (effective), Topical Vit.C, some herbals (cocoa butter).

III- Physical Methods

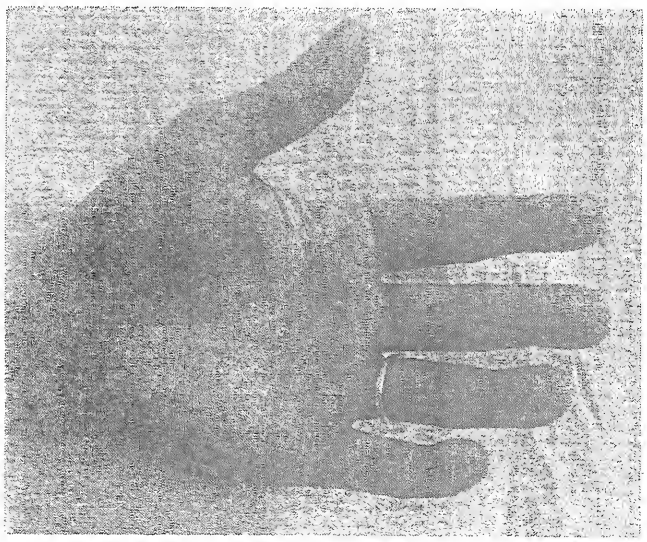
TCA and glycolic peel, PDL laser, CO2 laser, and Fractional laser.

Vascular changes

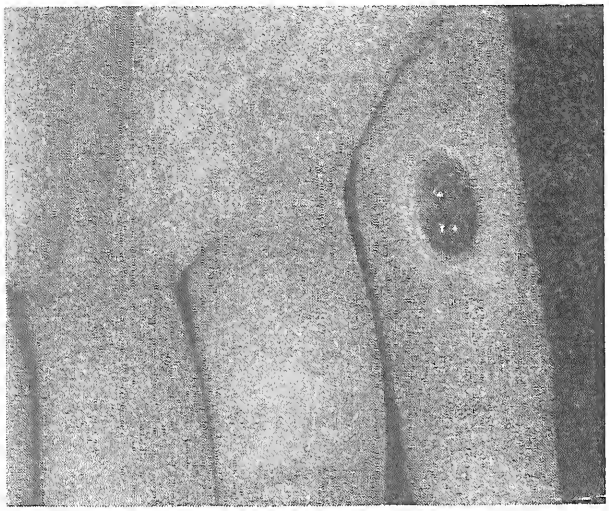
Spider Angioma

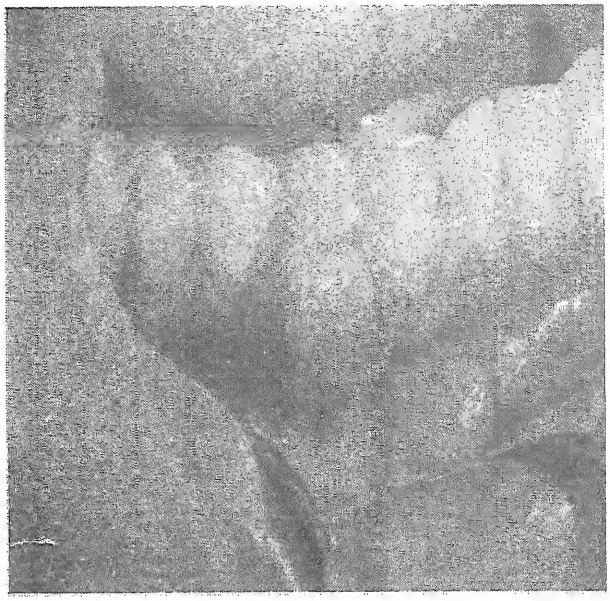


Palmar Erythema



Granuloma Gravidarun (Pregnancy tumor)



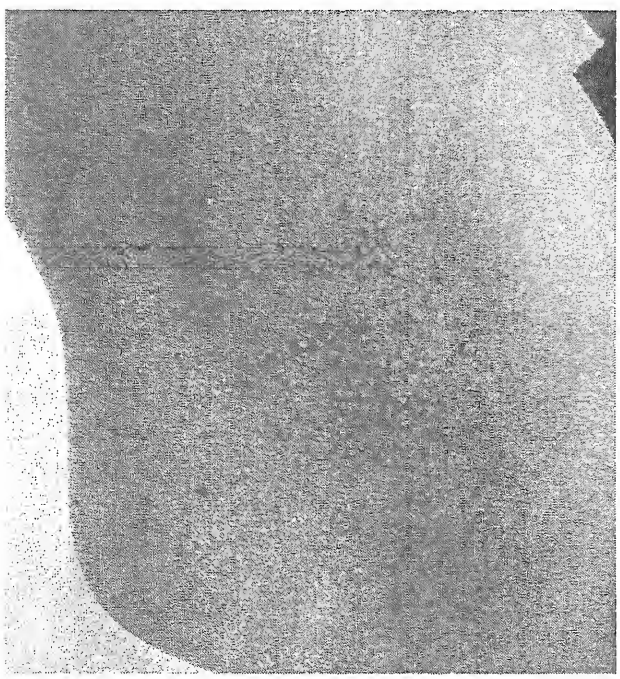


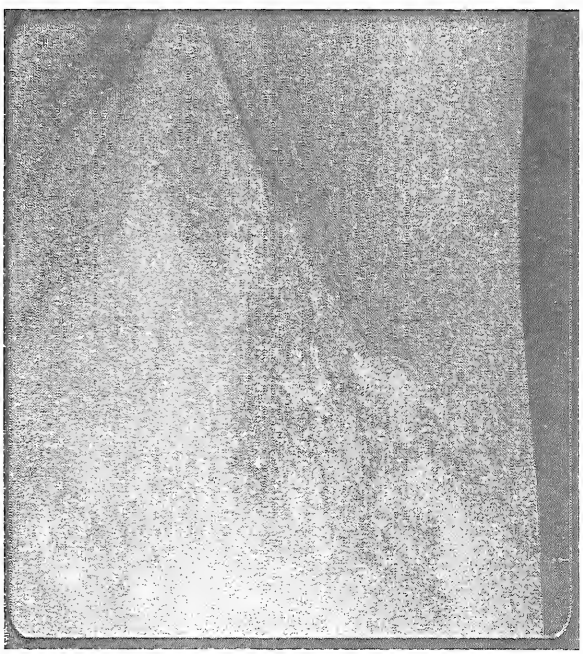
Gingival Hyperplasia

II- Dermatoses exacerbated or Improved during pregnancy

- Generally speaking; the disease improved may also exacerbate (no rule).
- **Th2 Mediated diseases:** will Exacerbate eg. Atopy, SLE
- **Th1 Mediated diseases:** Will improve eg. Psoriasis

Diseases that may improve are: Psoriasis, Fox-Fordyce & Hidradenitis

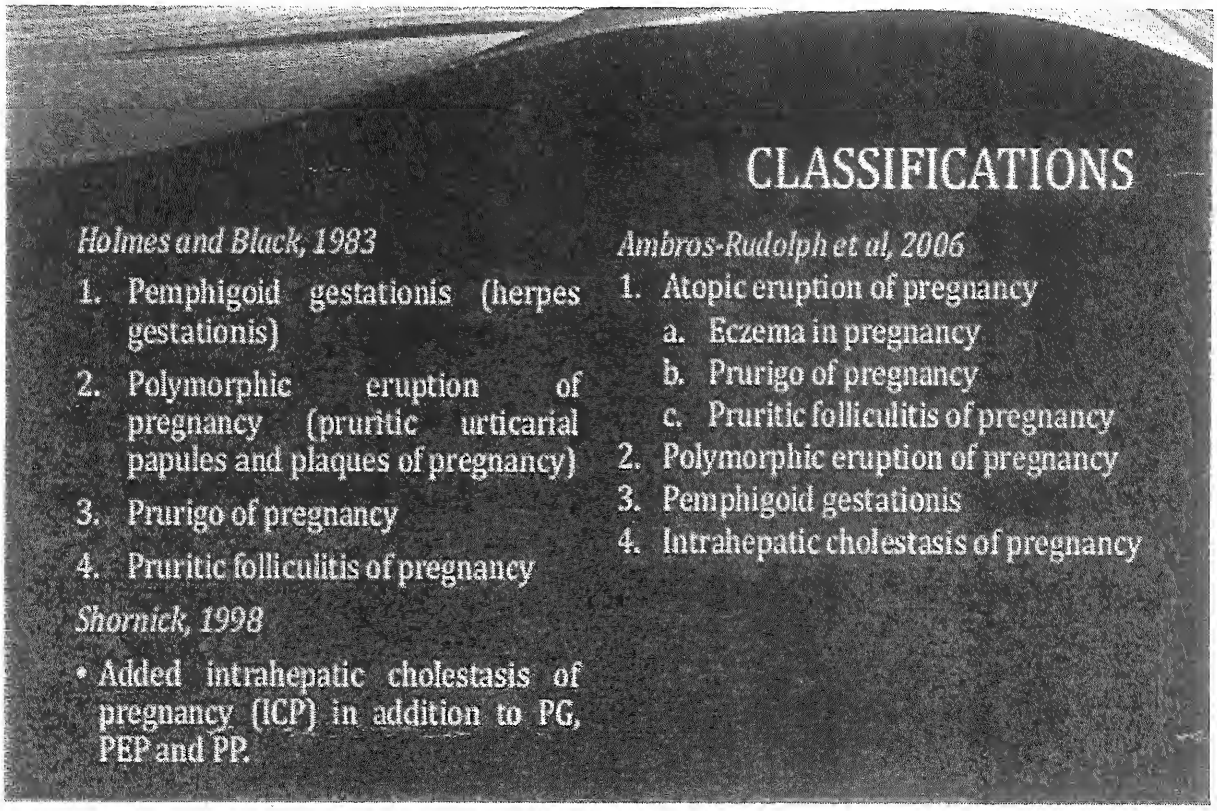




III- Specific Dermatoses of Pregnancy

- **Represent a heterogeneous group of severely pruritic inflammatory dermatoses associated exclusively with pregnancy or *the immediate postpartum period*.**

- **These dermatoses have been reclassified recently.**



Recent classification (JAAD,2006,Debated)

- Pemphigoid (Herpes) Gestationis (HG/BG)
- Polymorphic eruption of pregnancy (PEP)(*Old name:* PUPPP)
- Intra-hepatic cholestasis of pregnancy (IHCP) (Prurigo Gravidarum).
- Atopic Eruption of pregnancy (AEP) (*Old names*: Prurigo of pregnancy, and Pruritic folliculitis of pregnancy).

Clinical Approach, Itching during Pregnancy

Itching without Rash	Itching with Rash
Physiological Pruritus (50%)	- PEP/PUPPP
	- HG/BG
IHCP	- Atopic Eruption of (AEP,Prurigo of pregnancy)

Dermatoses Not Associated with Rash

Intrahepatic Cholestasis of Pregnancy (Prurigo gravidarum, IHCP)

- **Def.:** Hepatic condition that occurs during 3rd trimester and characterised by pruritus +/- jaundice(10%)
- **Incidence:** 3rd most common dermatosis of pregnancy.
- **Onset:** 3rd trimester (but +/- early at 8th week)
- **Pathogenesis:** ↓ Bile acids excretion → ↑ serum level → Cross the placenta → cause fetal anoxia & cardiac depression

C/P & Criteria

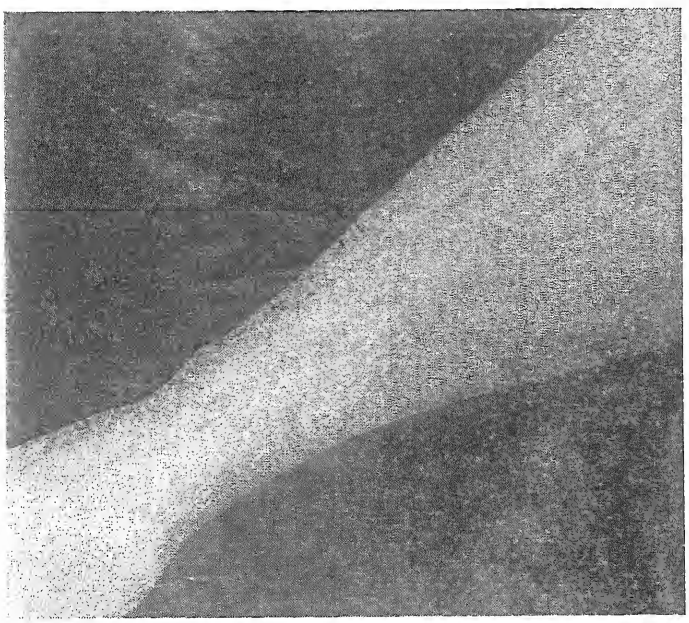
- **Generalised Pruritus:** ↑ ↑at night, involves face, palms and soles

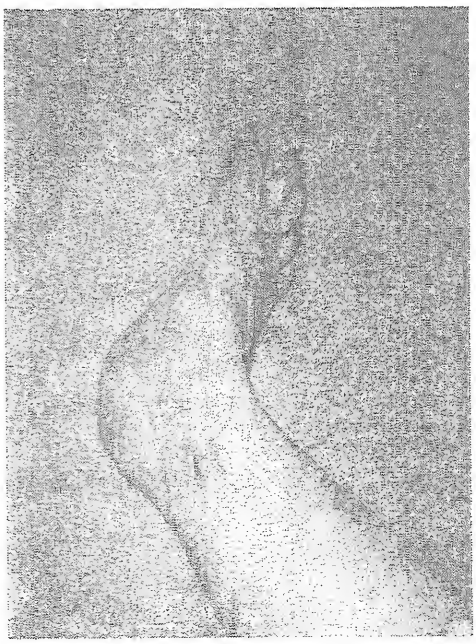
- **NO 1ry Skin Lesions** (only 2ry excoriations).

- **Jaundice** : 50%

- **Biochemical Abnormalities:**
  - ↑bile acids(الاهم علاطلاق) (total, cholic acid&chenodeoxy cholic)
  - SGPT (مهم)و↑total bilirubin, ↑SGOT
  - Alk.Phosphatase

IHCP





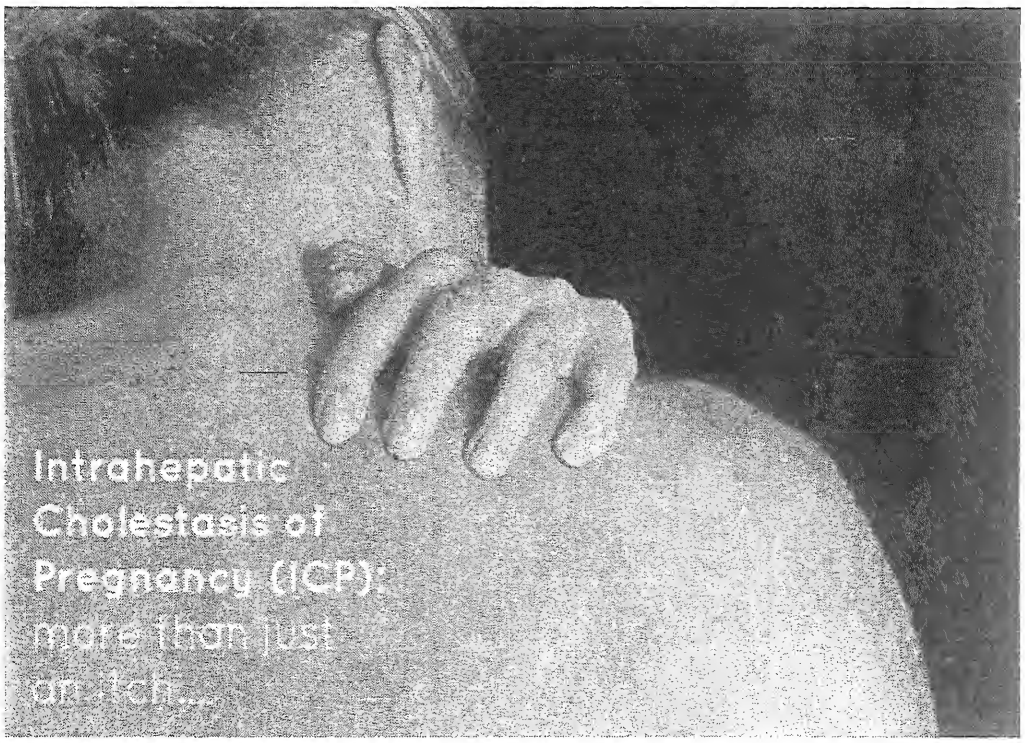
- **Resolution:** with delievery

- **Recurrence:** with subsequent pregnancy and OCPs.

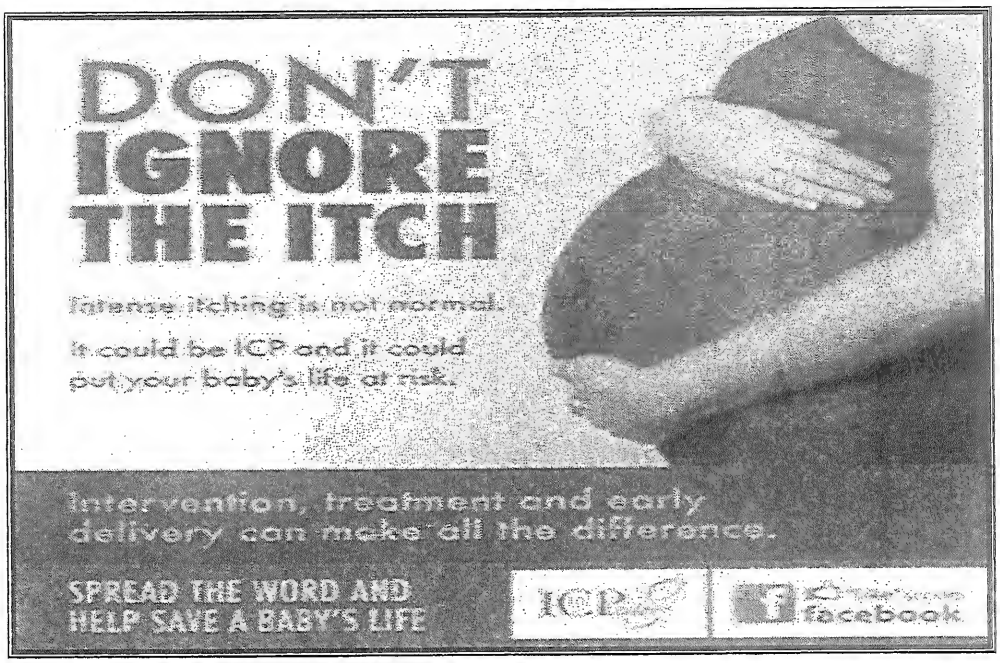
- **Complications**

  - **Maternal:** steatorrhoea,↓ Vit.K absorption, Gallstones, HEMORRHAGE

  - **Fetal:** IC hemorrhage, distress, stillbirth (1-2%),Cardiac Depression.



ICPcare™



IHCP,Treatment

- Bed rest , low fat diet
- Vit. K ,induction at 38 Ws gestation
- Ursodeoxycholic acid (15mg/kg)
  - Category B

Dermatoses Associated with Rash

Polymorphic Eruption of pregnancy (Pruritic Urticarial Papules and Plaques of Pregnancy) (PUPPP)

- **Incidence:** the 2nd most common specific dermatosis of pregnancy

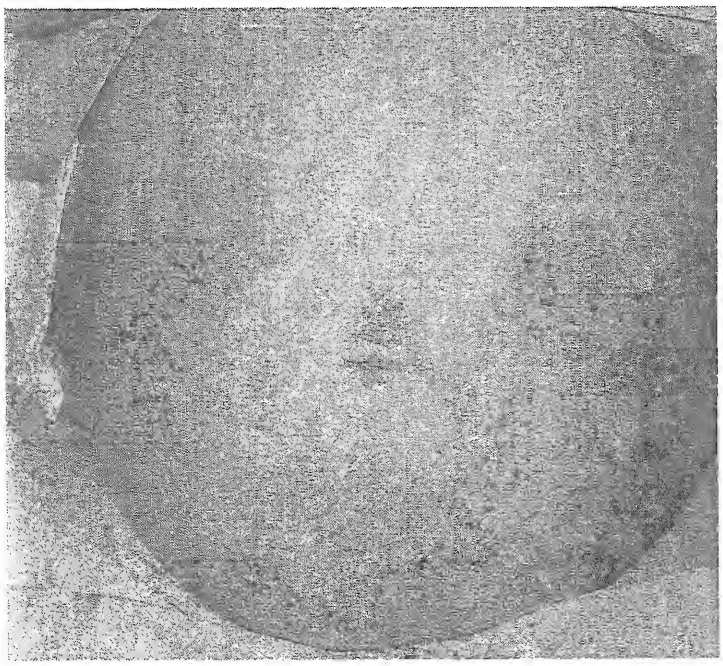
- **Etiopathogenesis:** ??, may be related to rapid and marked abdominal distension→ CT damage→ inflammation→ PUPPP

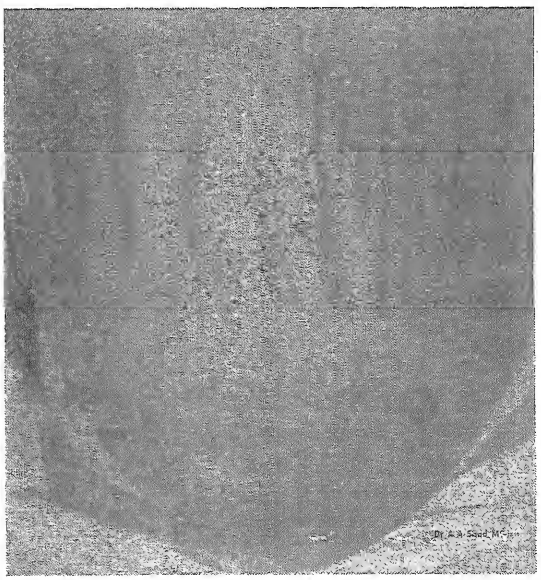
- **Risky Patient:** primigravida, 3rd trimester,twins, overweight baby and polyhidraminos.

- **Onset :**3rd trimester or immediate post-partum

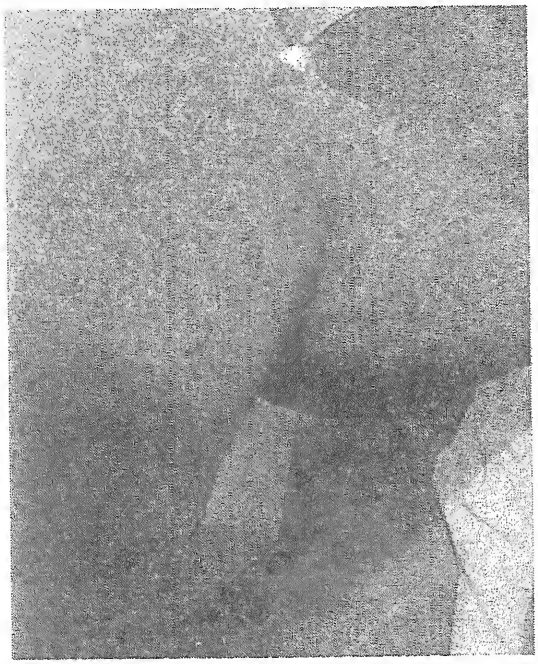
- **C/P:** severly itchy, PUPP (polymorphic lesions):Eczematous, targetoid lesions, vesicles (BUT NO BULLAE). Lesions start at STRIAE, then spread

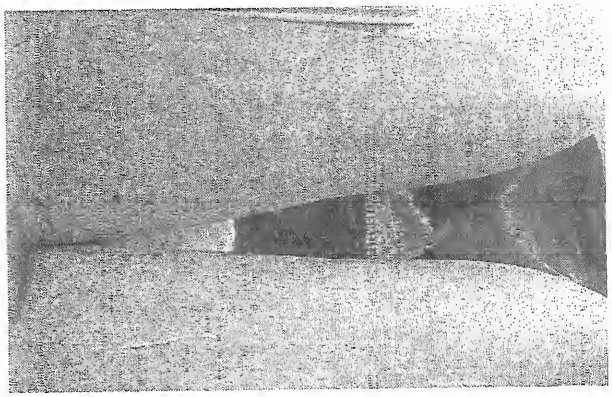
PUPPP





PUPPP





- **Resolution**: few days after delievery
- **Recurrence :** NO
- **Complications** :NO
- **Treatment:** (symptomatic)
  - Antihistamines
  - Topical Cs
  - Systemic Cs
  - NB-UVB

Pemphigoid (Herpes) Gestationis (PG)

- **Def.:** Self limiting autoimmune bullous disorder of mainly late pregnancy or postpartum.

- **Incidence:** Rare

- **Onset:** 3rd trimester or even postpartum.

NB: There is often a relative quiescence in late pregnancy, followed by a flare at the time of delivery or in the immediate postpartum period in 75% of cases.

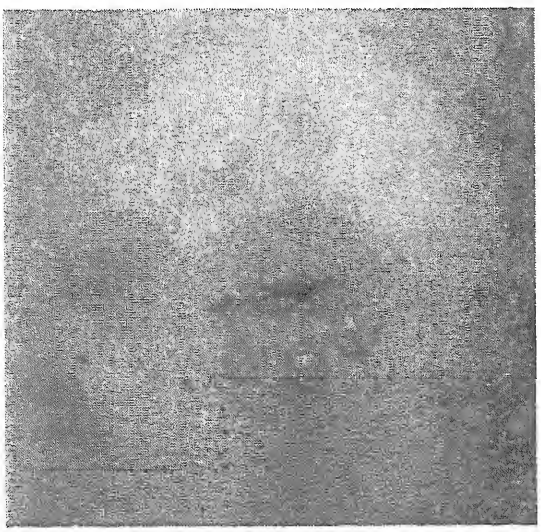
- **Etiopathogenesis:** Abnormal expression of class II HLA DR3, DR4 (paternally derived) at chorionic villi of placenta→ immune response initiation against placental BMZ Ag (HG Ag)→ IgG1 autoantibodies→ cross-react with cutaneous BPAg2 (180-kd) and BPAg1(230-kd) at BMZ

CP

- **C/P:** PUPP like lesions, targetoid lesions, usually start *PERIUMBILICALLY* → involve trunk,back,buttocks and arms →large, tense bullae+/-annular configuration

- **NB:**
  - There is sparing of Acral parts and MM(20 % only)
  - Sometimes NO blisters, only erythematous plaques and targetoids.

PG



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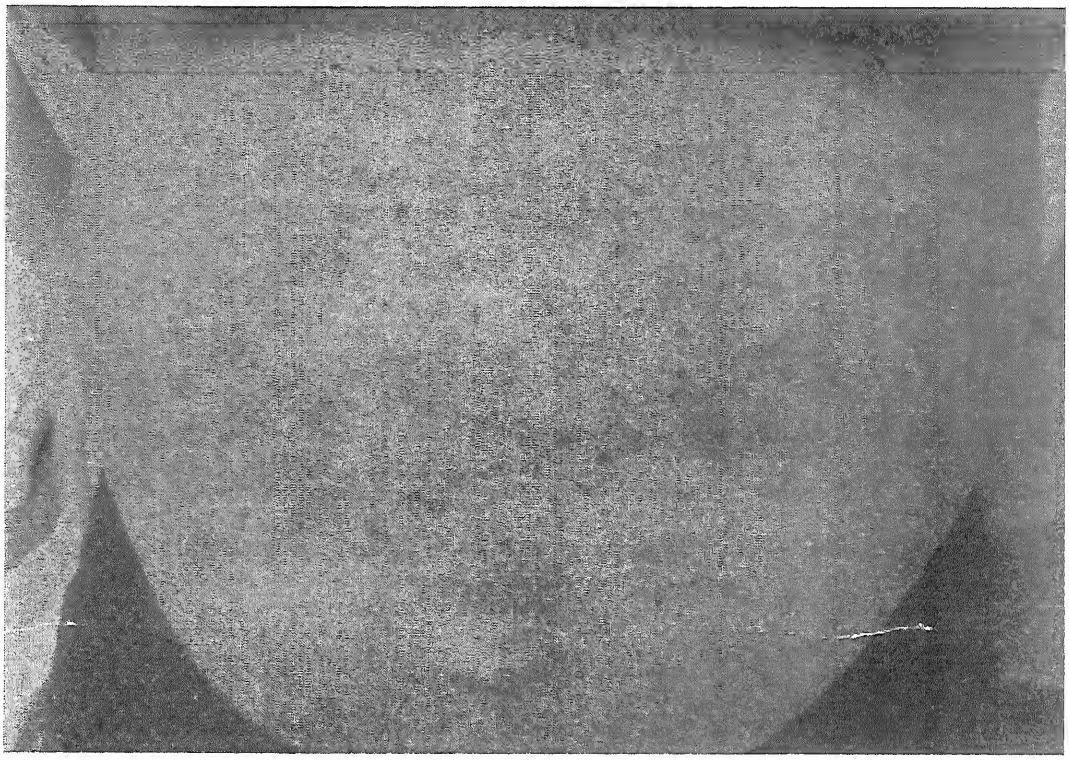
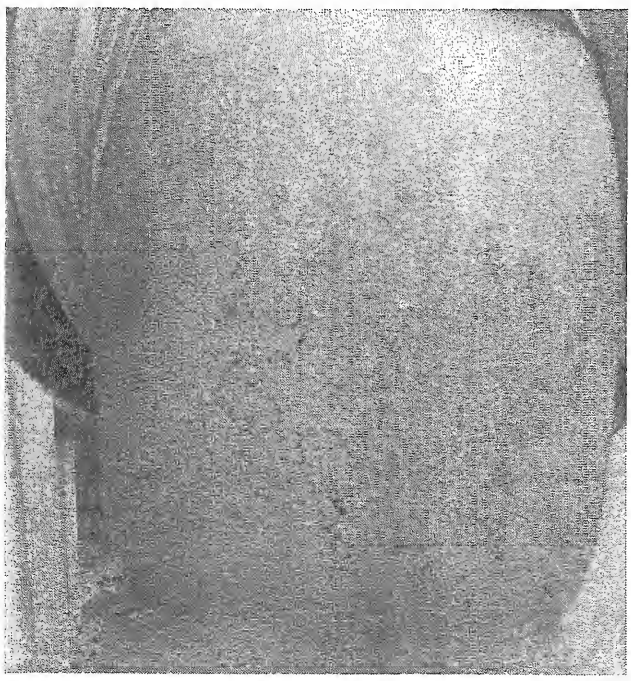
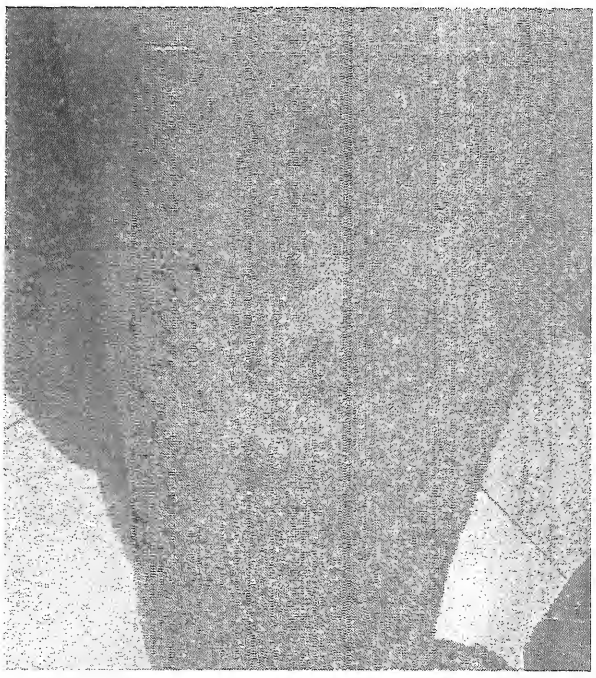
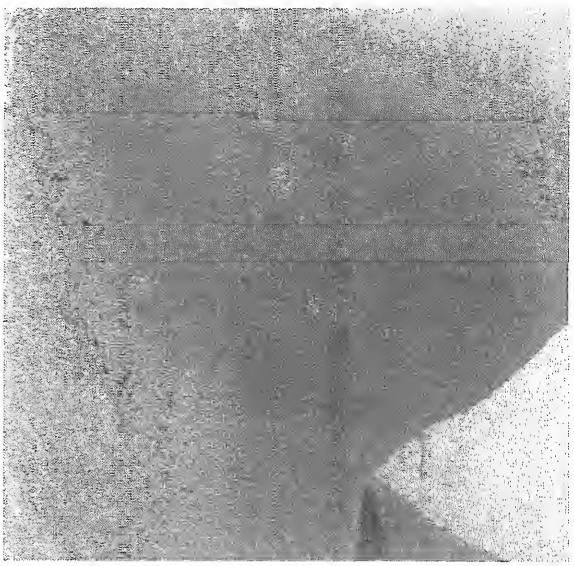


PG





PG



- **Resolution:** Postpartum, (Ws-Ms)

NB: Some cases has protracted course called chronic PG while others develops classical BP).

- **Recurrence:** with subsequent pregnancy, OCPs, vesicular mole or choriocarcinoma.

NB: '*Skip pregnancies*', however, have been reported (8%) and were attributed to a male consort (قرين) change or expression of identical HLA-DR antigens by mother and fetus.

- **Diagnosis:**
  - **HP**: subepidermal blisters with eosniophilic infilt.
  - **DIF**: Linear C3, IgG at L.L of BMZ.
  - **IIF:** IgG autoantibodies against BP Ag2 and BP Ag1

- **Complications:**
  - **Maternal:** BP (some case)
  - **Fetal**: PG, Prematurity, LBW, Neonatal BP (10%, due to maternal transfer of autoantibodies).

- **Treatment:**
  - **Mild HG:** Antihistamines , Dermovate
  - **Severe HG**: Systemic Cs.

PUPPP *Vs* PG

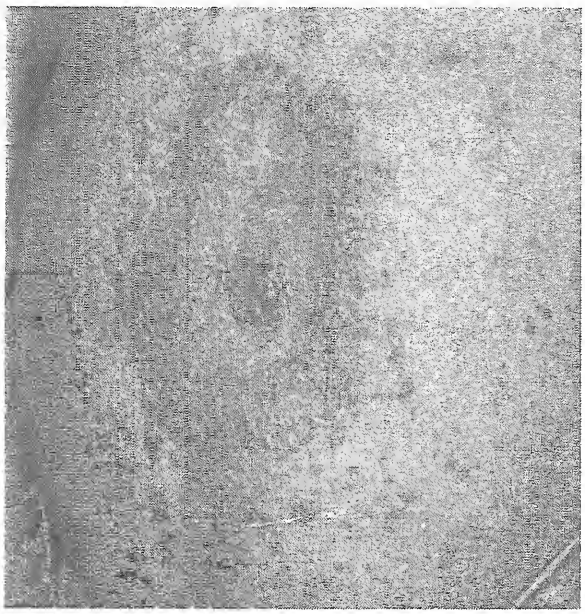
- **Both:** at 3rd trimster or postpartum

- **PUPPP:**
  - Primigravida
  - At striae.
  - Lesion may be targetoid or vesicular (NO BULLAE).
  - NO complications
  - NO recurrence

HG:

- Sarts Periumblically
- PUPP then become bullous.
- Lesion may be targetoid or remain NON BULLOUS.
- Complicated
- Recurrent

So the periumbilical area is considered as a land- mark in diagnosis of both PUPPP (free only striae) & HG (involved)



Atopic Eruption of Pregnancy (AEP) (Prurigo of pregnancy)

- **Incidence:** AEP is the most common dermatosis of pregnancy, accounting for 50% of pregnancy specific dermatoses

- About 20% of women experience an exacerbation of pre-existing eczema in pregnancy, whereas 80% experience atopic skin changes for the first time or after a long remission (for example, since childhood)

- **Etiopathogenesis:** immunosuppression with predominance of TH2.

- **Onset:** Before the 3rd trimester (بدري عن باقي الانواع)

- **Types :**

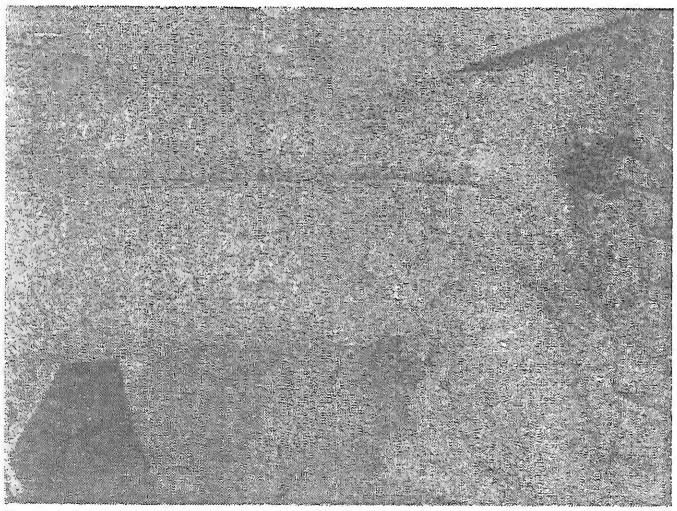
  - **Eczematous type (papular dermatitis of pregnancy)(2/3 cases):** 1st& 2nd trimester, eczematous changes affecting typical atopic sites such as the face, neck and flexures

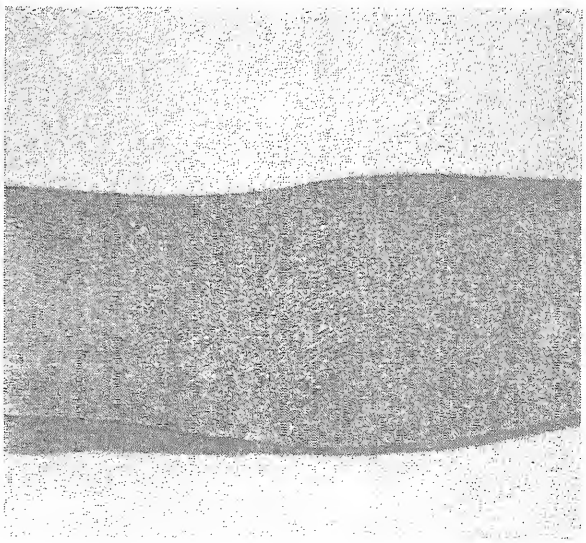
  - **Papular type (Prurigo of pregnancy) (1/3 cases)**

  - **Pruritic folliculitis of pregnancy.**

- **Resolution:** Postpartum
- **Recurrence :** With subsequent pregnancy
- **Complications:** NO maternal, may be fatal Atopy

AEP (Eczematous)



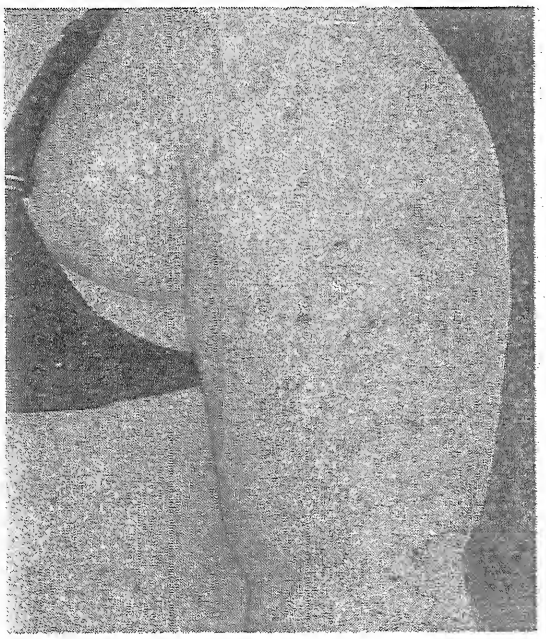


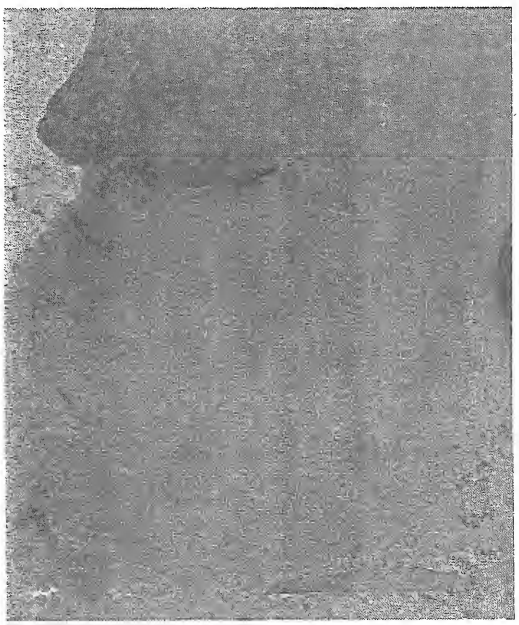
Prurigo of pregnancy
(Not Prurigo Gravidarum)

Itchy, Excoriated, Papules and Nodules (prurigo nodularis like), at Extensors and Trunk

- **Onset:** 2nd or 3rd trimester
- **No** complications
- +/- Recurrence
- **Symptomatic** treatment

AEP (Papular/Prurigo of pregnancy)



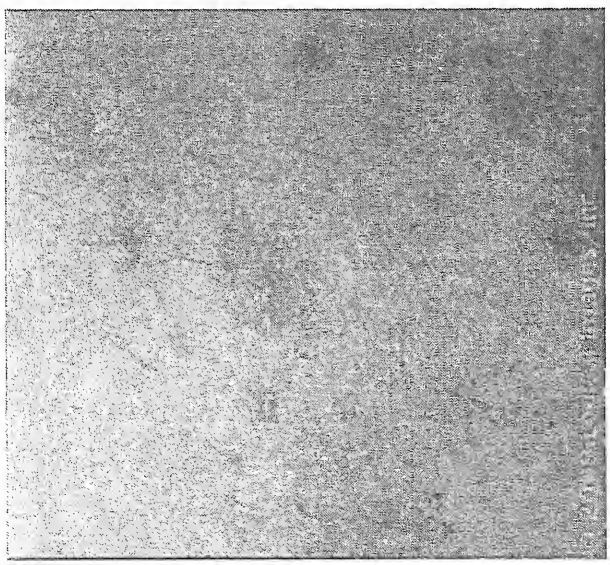


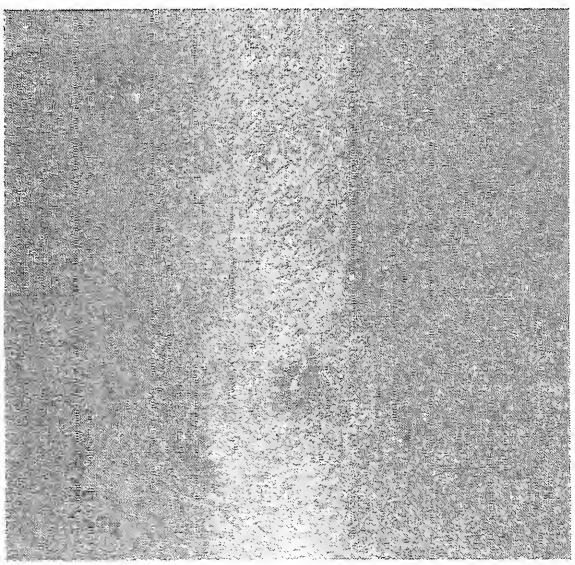
Pruritic folliculitis of pregnancy

Itchy, follicular papules and Pustules at Trunk and Extremities (Acneiform like eruptions)

- **Etiopathogenesis:** a form of hormonally induced acne, similar to steroid acne
- **Onset:** 2nd or 3rd trimester
- **No** complications
- **+/-Recurrent**
- **TTT:** Topical Cs, antihistamines or UVB

Pruritic folliculitis of Pregnancy





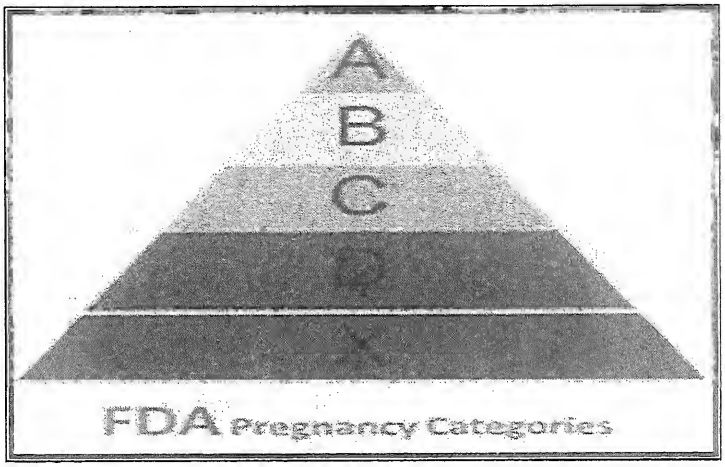
Other Dermatoses: Unclassifies

- Impetigo herpetiformis (pustular Psoriasis of pregnancy)
- Autoimmune progesterone dermatitis
- Linear IgM dermatosis (Non specific dermatosis, characterized by:follicular papules&pustules that show Linear IgM by DIF

Autoimmune Progesterone Dermatitis

- Though, non specific for pregnancy , but it may appear for first time during it
- Eczematous, urticarial&EM-like rash during Luteal phase of cycle
- Diagnosis: Intradermal injection of progesterone→ urticaria within 30 mins. Or Erythematous induration within 1-2ds
- TTT: Stop ovulation (Estrogen only pills, Tamoxifen&Danazol)

Dermatological Drugs & Pregnancy



FDA Categorization of Drugs during Pregnancy

Category	Definition	Animal studies	Human studies
A	No risk in controlled studies	-ve	-ve
B	No proven risk	-ve	No data
		+ve	-ve
C	Risk can't be ruled out	+ve	No data
		No data	No data
D	Evidence of risk	-ve or +ve	+ve
X	Sure risk, Absolute contraindication	+ve	+ve

FDA Categorization

FDA pregnancy drug class

Class	Clinical implication	Example
A	No risk to fetus	Vitamin B6
B	No evidence of risk	Brimonidine, azithromycin, erythromycin, tobramycin
C	Risk to fetus cannot be ruled out	Ciprofloxacin, other glaucoma medications, corticosteroids, dilating agents
D	Risk to fetus, but benefits may outweigh risk	Tetracycline, doxycycline
X	Definite risk; Avoid	Misoprostol

Source: Food and Drug Administration

Antihistamines & Pregnancy

- **<u>Sedating Antihistamines:</u>**

All are category (B) except hydroxyzine (Atarax) and Doxepine are (C).

- **<u>Non sedating Antihistamines:</u>**

All are category (B) except fexofenadine and desloratadine are (C)

However; cumulative experience with sedating types are greater, so chlorpheniramine (Avil, anallerge) is the safest during pregnancy

Systemic Cs & Pregnancy

- **Category:** C
- **1st trimester:** Cleft Palate
- **Others:** LBW and Placental Calcification